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## CONTENTS

## Original Communications

Experimental Observations on the Surgical Treatment of Hypertension. Harry Goldblatt, M.D., C.M., Cleveland, Ohio	483
Some Aspects of Blood Pressure Regulation and Experimental Arterial Hypertension. O. Heymans, M.D., Ghent, Belgium	487
Essential Hypertension: The Selection of Cases and Results Obtained by Subdiaphragmatic Extensive Sympathectomy. W. McK. Craig, M.D., Rochester, Minn.	502
Blood Potassium During Experimental Shock. Raymond L. Zwemer, Ph.D., and John Scudder, M.D., New York, N. Y.	510
Studies of Sodium, Potassium, and Chlorides of Blood Serum in Experimental Traumatic Shock, Shock of Induced Hyperpyrexia, High Intestinal Obstruction, and Duodenal Fistulas. J. Dewey Bisgard, M.D., A. R. McIntyre, M.D., and W. Osheroft, M.D., Omaha, Neb.	528
The Survival of Clostridium Sporogenes, Bacillus Subtilis, and Staphylococcus Albus on Surgical (Catgut) Ligatures. Katherine E. Hite, B.S., and G. M. Dack, M.D., Ph.D., Chicago, Ill.	548
Treatment of the Undescended Testis: With Special Reference to Therapy With Hormones. Charles E. Rea, M.D., Minneapolis, Minn.	552
Primary Retroperitoneal Tumors. Robert T. Frank, A.M., M.D., New York, N. Y.	562
Hypertrophy of the Ligamentum Flavum. J. M. Meredith, M.D., and Edwin P. Lehman, M.D., University, Va.	587
Subcutaneous Injuries of the Intestine and Mesentery. H. P. Totten, M.D., Los Angeles, Calif.	597

## Editorial

Gas Bacillus Infection. L. Sidney Charbonnet, Jr., M.D., New Orleans, La.	610
---------------------------------------------------------------------------	-----

## Recent Advances in Surgery

Salt Balance in Surgical Patients. Robert M. Bartlett, M.D., Dermid L. C. Bingham, F.R.C.S. (Ed.), and Svend Pedersen, Ph.D., Ann Arbor, Mich.	614
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## Review of Recent Meetings

The American Proctologic Society. Curtlee Rosser, M.D., Dallas, Tex.	636
Report of the Section on General and Abdominal Surgery of the Meeting of the American Medical Association, San Francisco, Calif., June 13-17, 1938. Leon Goldman, M.D., San Francisco, Calif.	639



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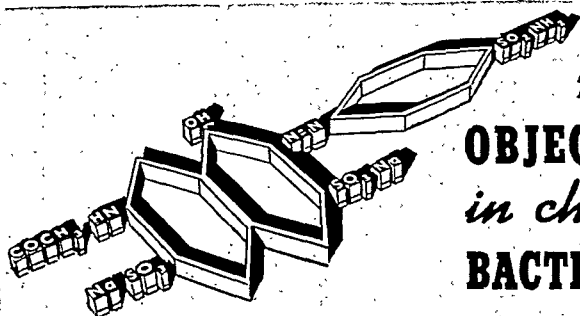
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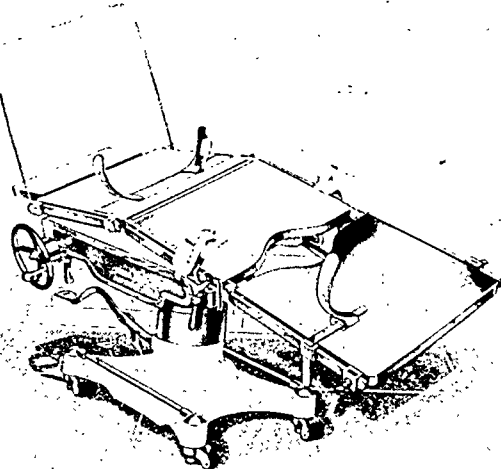
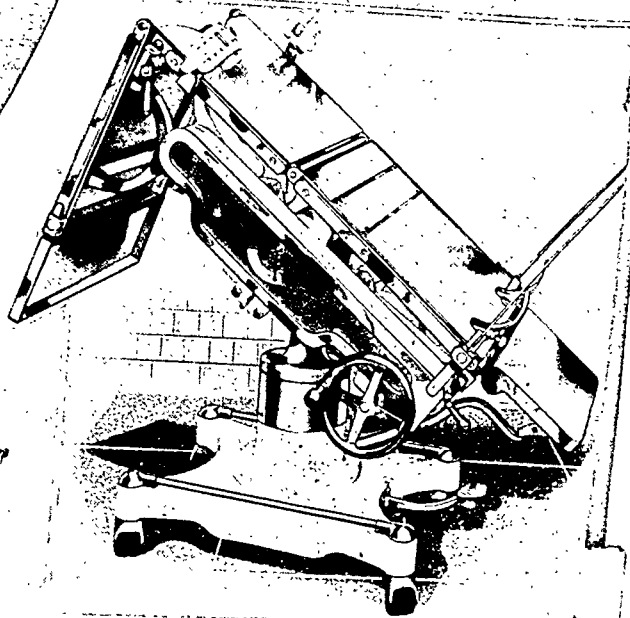
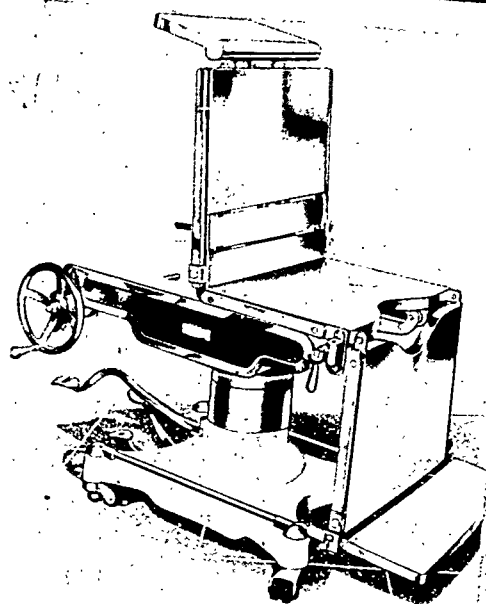
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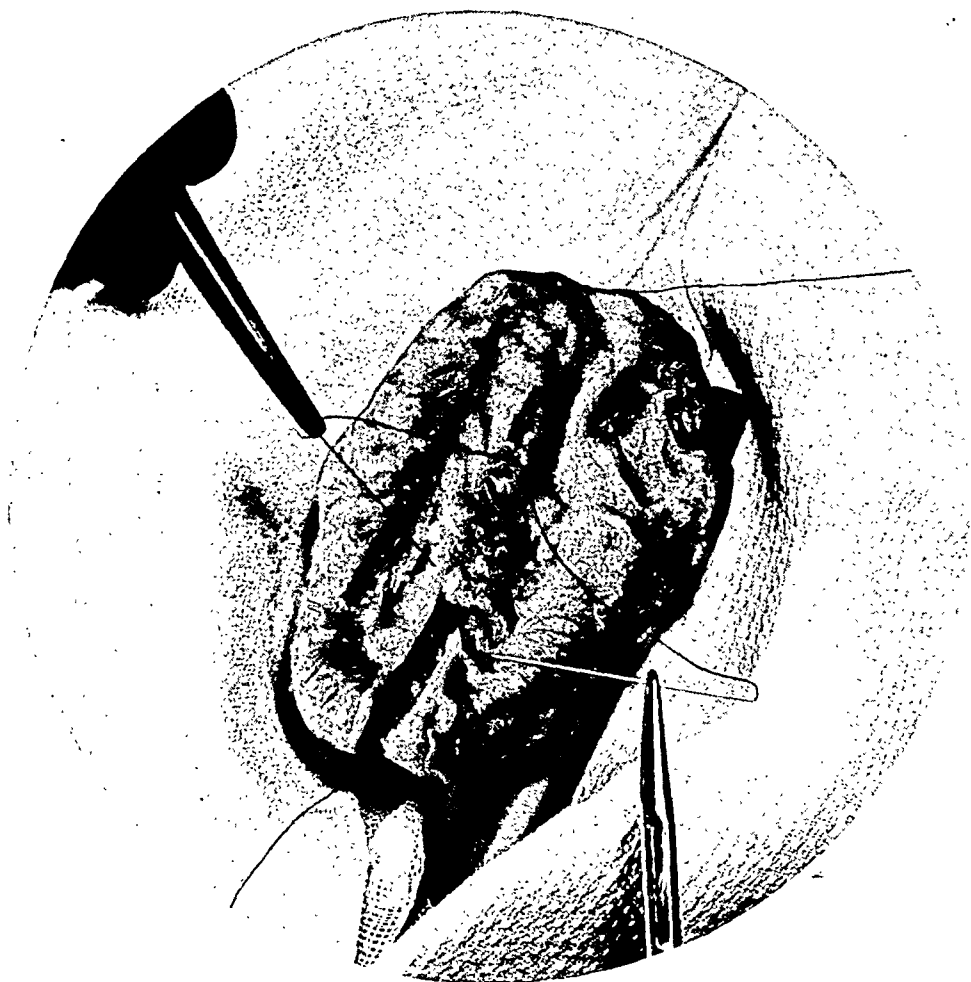
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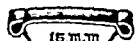
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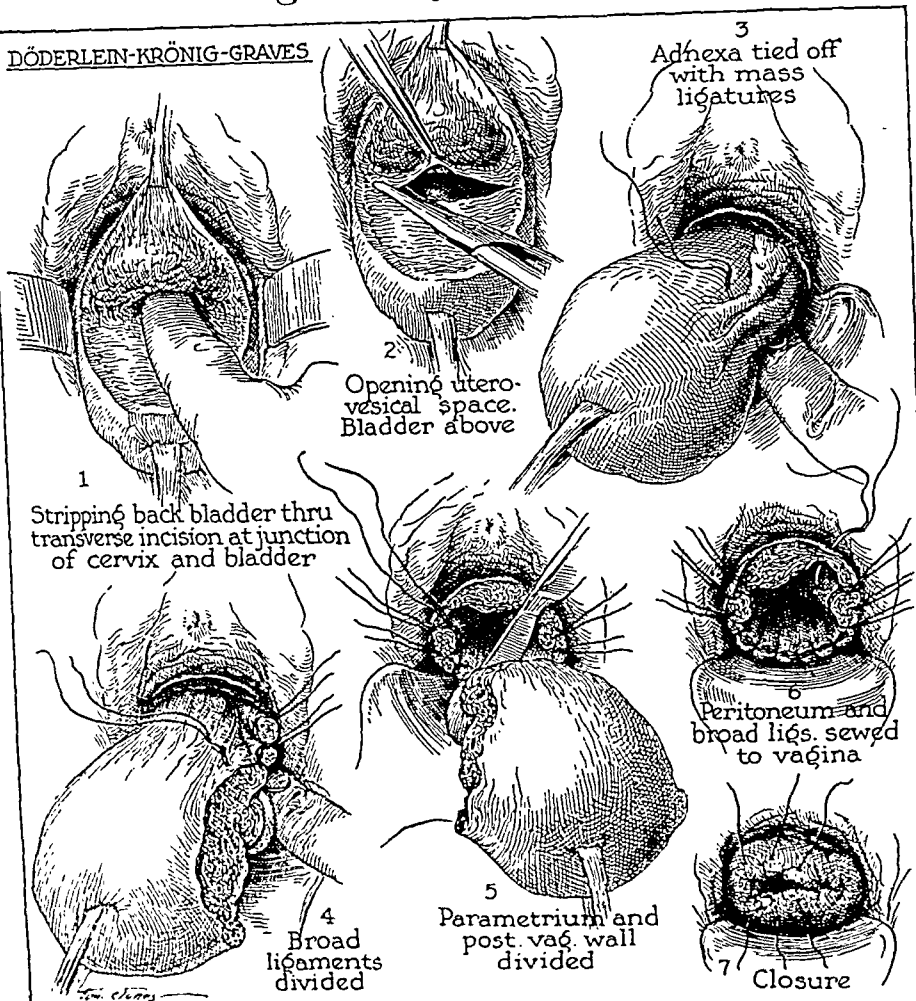
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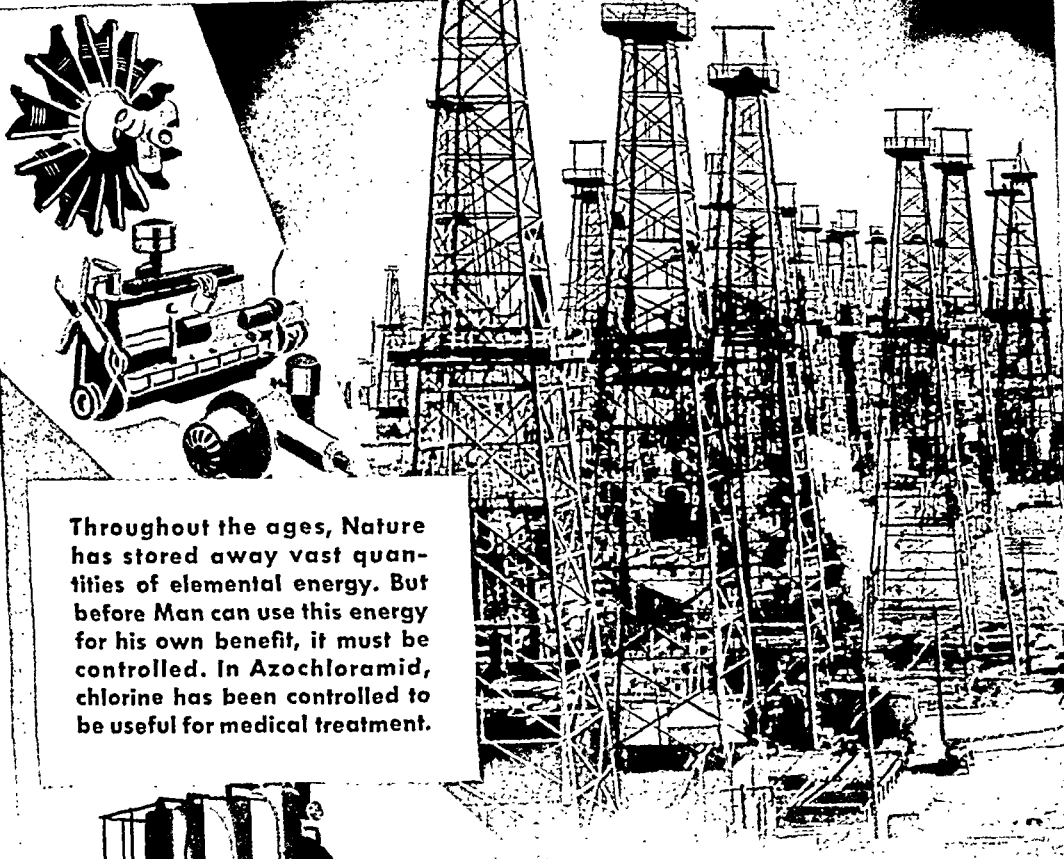
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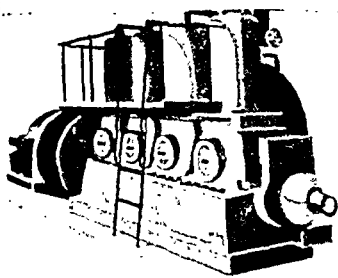


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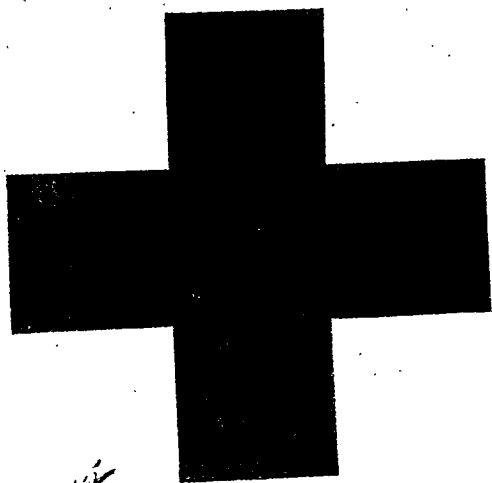
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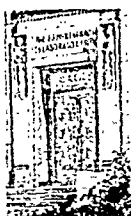
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# SURGERY

VOL. 4

OCTOBER, 1938

No. 4

## Original Communications

### EXPERIMENTAL OBSERVATIONS ON THE SURGICAL TREATMENT OF HYPERTENSION\*†

HARRY GOLDBLATT, M.D., C.M., CLEVELAND, OHIO

IN RECENT years surgical treatment of hypertension has come to the fore. This has consisted of denervation of some organs or section of nerves and excision of ganglia connected with the vasomotor apparatus of the abdomen. Denervation of the adrenals or kidneys, section of splanchnic nerves, section of anterior nerve roots, and excision of celiac or lumbar ganglia have been the operations of choice. Some of these procedures have been combined with unilateral or partial bilateral adrenalectomy. Irradiation of the adrenals by roentgen rays and partial adrenalectomy alone also have been tried. It is interesting to note that some of the methods which were regarded as effective at first were discarded later as useless even by the originators. It is also noteworthy that only the originators of each operation have been enthusiastic about the beneficial effects of their operation and have reported poor success or failure with other methods. As in the case of other methods of treatment, factors other than the level of the blood pressure, such as disappearance of headache, and other subjective symptoms have been used in the evaluation of the effect of the treatment. The unreliability of such criteria need not be stressed. It is a striking fact that no matter what the type of surgical operation on the nervous system, the percentage of cases in which a significant lowering of the blood pressure has been reported is about the same for all. After all the operations the percentage of cases in which there is a return of the blood pressure to normal is relatively small.

In evaluating the benefit of any surgical treatment, one must not forget the possible effect of the period of enforced rest which is involved in

\*These studies were supported by the Beaumont-Richman-Kohn Fund and by special grants-in-aid from the Josiah Macy, Jr., Foundation, Mr. Nathan Dauby, and Mr. Alex Wintner and associates of Cleveland, Ohio.

†From an address delivered as part of a symposium at the second Louis A. Greensfelder Memorial Lectureship, Michael Reese Hospital, Chicago, Ill., Nov. 23, 1937.

Received for publication, May 2, 1938.

the operation and of the restriction of activity which follows. An explanation of the remainder of the beneficial effect in some cases is suggested by the investigations that have been made on the effect of the same operations on experimental hypertension due to renal ischemia. Briefly, this type of hypertension\* can be produced at will by constricting both main renal arteries by means of a special clamp or by constricting the main artery of one kidney and at the same time, or later, removing the other kidney. It also can be accomplished by constricting the aorta above both renal arteries. If the constriction of the main renal arteries is moderate, but adequate, the blood pressure remains elevated, and there is little or no accompanying disturbance of renal function, although the hypertension persists for years. After several years of hypertension, the small arteries and arterioles show some thickening of the media and sometimes slight hyalinization of the intima, especially in retinal arterioles. This type is similar to the benign phase of human essential hypertension. If the constriction of the renal arteries is made severe, there follows hypertension and reduced renal function which may lead to fatal uremia. The arterioles of many organs show severe changes, such as hyalinization, fibrinoid degeneration, and necrosis. This type resembles the acute malignant phase of human essential hypertension. It is upon experience with the treatment of these two types of experimental hypertension that the comments on the surgical treatment of human hypertension are based. All of the operations on the nervous system that have been performed on man have also been carried out on animals without any effect in preventing or permanently lowering this type of experimental hypertension. In the animals more extensive operations have also been carried out. Total sympathectomy of thorax and abdomen and even pithing have had no effect on this type of experimental hypertension. The effect on the vasomotor apparatus is presumably the same as in man. There is, however, one notable difference between the two. In the animals the restriction of blood to the kidneys is effected by constriction of the main renal arteries by means of a rigid clamp. This is not altered by any of the operations on the nervous system. In man, on the contrary, the counterpart of the effect of the silver clamp is produced by the constriction or thickening of the wall of the arterioles of the kidney. It is conceivable, at least, that some of these vessels are merely in spasm and still under the influence of the nervous system and that they are, therefore, in a reversible state and can become dilated as a result of removal of the vasoconstrictor effect. The conclusion that follows from these experiments is that what improvement does occur from these operations, in all probability is, apart from the

\*For complete bibliography, see Goldblatt, Harry: *Experimental Hypertension Induced by Renal Ischemia*, Harvey Lectures, Baltimore, 1937-38, Williams and Wilkins, Vol. 33.

effect of enforced rest, due to the improvement of the circulation through the kidneys and not to any effect on the rest of the vasomotor apparatus of the abdomen.

As concerns interference with the adrenals, one can merely state that the experimental work up to the present time shows that removal of the medulla of both adrenals has no significant effect in preventing or lowering blood pressure. This decreases materially the probability that epinephrine plays any part in the phenomenon. It has been found that experimental hypertension due to renal ischemia is not prevented or lowered by partial adrenalectomy, unless the amount of the cortex left is inadequate to support life. There is, therefore, no experimental basis for any surgical or other physical interference with the adrenals in the treatment of hypertension. It seems fair, in the circumstances, to sound a note of warning about this method of treatment which is still being practiced by some surgeons.

One obvious surgical therapeutic procedure which suggests itself as the result of this work is the possible improvement of blood supply to the functioning components of the kidney by increasing the collateral circulation. In the animals with experimental hypertension induced by renal ischemia, whenever there is a return of the blood pressure to a lower level, it is due to inadequate initial clamping of the renal arteries or to the development of effective accessory circulation by way of ureteral and capsular vessels, which may become very prominent. If, before constricting the renal artery, the kidney is decapsulated and adipose tissue or muscle is attached to the denuded cortical surface, the accessory circulation from the adherent tissues becomes very prominent and interferes with the development of pronounced elevation of blood pressure. Since, in the animals, the constriction is only of the main renal artery, such accessory circulation can be of functional significance. The fact that animals have survived several years the complete closure of both main renal arteries, when effected gradually, by increasing the constriction at intervals, is proof that such accessory circulation can be functionally highly effective. However, in human essential hypertension, the vascular disease most frequently involves also the afferent preglomerular arterioles, so that collateral communication with the larger vessels would not improve circulation to glomeruli. Whether improvement of blood supply to some glomeruli, to tubules and interstitial tissue would occur as a result of renal decapsulation and attachment of omentum, muscles, or other tissues to the surface of the kidney, and whether it would be effective in lowering blood pressure in human essential hypertension cannot be determined without trying this type of operation. Although I have hesitated to recommend it, yet there is probably more justification on an experimental basis for making this test than there has been for some of the surgical procedures that have already been practiced. The cases in which the surgical production of



accessory circulation would be most effective would be those in which the hypertension is due to sclerosis of the main renal arteries alone or their very large branches. The difficulty of making a diagnosis of this condition is obvious, so that unless the method could be applied to essential hypertension associated with renal arteriolar sclerosis the procedure would be of greatly restricted value.

An interesting recent practical application of this work, which centers upon the renal origin of so-called essential hypertension, has been the finding in children and adults of hypertension associated with unilateral pyelonephritis and vascular disease, and the prompt return of the blood pressure to normal after excision of the diseased kidney. Until 1930, according to Bell and Pedersen, hypertension associated even with bilateral pyelonephritis had not been reported. Since then, Longcope and others have reported the occurrence of hypertension in some cases of bilateral pyelonephritis, and, from the meager studies of the kidneys, in these and in the cases of unilateral disease it has become probable that the hypertension associated with this condition in children and adults occurs only when there is associated vascular sclerosis or when the inflammatory disease produces the same effects on renal circulation as does vascular disease. In cases of unilateral arteriolar nephrosclerosis with hypertension, which have been reported by Moritz and Oldt, if the diagnosis could be made in life, removal of the diseased kidney might result in a return of the blood pressure to normal, as in the cases of unilateral pyelonephritis.\* Unfortunately, unless the production of accessory circulation would be effective, nothing but transplantation of a normal kidney or kidneys, with the removal of both diseased kidneys, could be expected to relieve the hypertension associated with bilateral pyelonephritis or bilateral arteriolar sclerosis of the kidneys.

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\*From the James Buchanan Brady Urological Institute and Department of Medicine of Johns Hopkins Hospital, there have just been reported two cases of hypertension associated with unilateral renal vascular disease in which the removal of the diseased kidney resulted in a prompt return of the blood pressure to normal. A similar result has been obtained in a third unreported case (personal communication from Prof. Hugh Young).

## SOME ASPECTS OF BLOOD PRESSURE REGULATION AND EXPERIMENTAL ARTERIAL HYPERTENSION\*

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FOR many years physiologists have been occupied with the study of the mechanisms which regulate blood pressure. A precise and detailed knowledge of the physiologic regulation of endovascular pressure is the key, not only to the physiology of normal circulation, but perhaps also to the pathogenesis of chronic arterial hypertension.

It is known that the arterial pressure is largely controlled by the activity of the heart, the cardiac rate, the cardiac output, the circulating blood volume, and, mainly, by the peripheral vascular resistance, the vasomotor tone.

The arterial pressure is dependent upon factors which are essentially labile and variable. In spite of the numerous influences which, in an unbalanced physical system, would cause extreme variations in pressure, fluctuation of mean blood pressure under differing conditions is strikingly limited. In may be asked, therefore, what are the mechanisms which prevent such fluctuations and maintain and adjust the blood pressure in this precise and sensitive manner so as to control and regulate the circulation and nutrition of the cells, tissues, and organs of the body.

In recent years experimental investigations have demonstrated that the regulation of blood pressure is essentially and fundamentally an *automatic, proprioceptive reflex mechanism*. In fact, the endovascular pressure itself regulates automatically the cardiac output, the circulating blood volume, and the peripheral vascular resistance so well that the arterial pressure is maintained within or quickly restored to normal limits. This *homeostasis of the arterial pressure* is effected mainly by the intermediation of the pressoreceptor innervation of different arterial and venous vascular areas.

The early experiments of v. Oyon and Ludwig,<sup>1</sup> as well as the more recent researches of v. Anrep and Starling,<sup>2</sup> Ladon and myself<sup>3,4</sup> and De Burgh Daly and Verney<sup>5</sup> have shown that the cardioaortic vascular zone, especially the aortic arch, is provided with a pressoreceptive reflexogenic innervation (Fig. 1). When the endovascular pressure rises

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in the left heart or aortic arch, impulses ascend centripetally along the cardioaortic nerves, inducing reflex cardiac slowing, diminution of cardiac output, and peripheral vasodilatation. On the other hand, when this endovascular pressure falls, the same pressoreceptors induce reverse vasomotor and cardiac reactions, characterized by vasoconstriction, cardiac acceleration, and an increase of cardiac output. These reflexes tend to keep a balance between hypertension and hypotension and to maintain normal arterial pressure.

One knows further from the work of Cooper,<sup>7</sup> Marey,<sup>8</sup> Francois-Franck,<sup>9</sup> and Hedon<sup>10</sup> that variations of carotid-cephalic arterial pressure immediately produces cardiac and vasomotor reactions. Carotid-

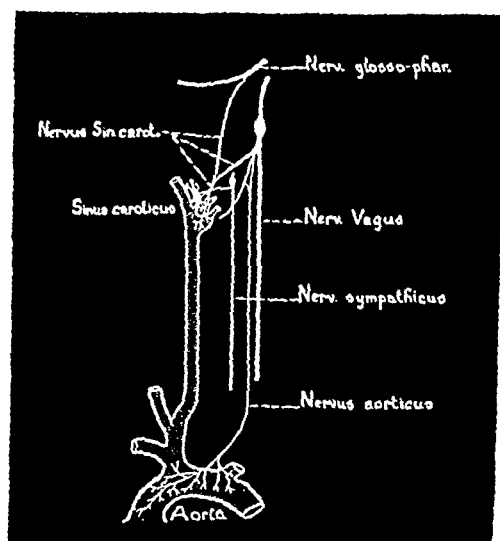


Fig. 1.—Diagram of the cardioaortic and carotid sinus pressosensitive innervation.

cephalic hypotension produced by clamping both carotid arteries induces acceleration of the heart, increase of cardiac output, and somatic vasoconstriction. The opposite phenomena, namely, cardiac slowing and somatic vasodilatation, are responses to carotid-cephalic hypertension. This mechanism of regulation of blood pressure was long attributed to the *direct* central influence of changes of blood pressure acting on the tonus of the cardiovascular centers.

The work of Czermack<sup>11</sup> and Coneato<sup>12</sup> and the observations of Sollmann and Brown<sup>13</sup> showed, however, that the common carotid artery, particularly its bifurcation, may be the origin of cardiovascular reflexes elicited by mechanical manipulation, such as by compression of the neck in the region of the carotid bifurcation or by traction on the cephalic end of the carotid artery.

The experiments of Pagano<sup>14</sup> and Siciliano<sup>15</sup> in 1900 had already seriously damaged the concept of direct, central automatic regulation of blood pressure. But their experiments, which were incomplete and contradicted by Kaufmann,<sup>16</sup> passed almost unnoticed, and the classical theory of the direct central regulation of blood pressure was still accepted until 1924 when new investigations, performed mainly in the laboratory of Hering<sup>17, 20</sup> and in our laboratory,<sup>4, 5</sup> clarified the forgotten observations of Pagano and Siciliano and revealed the existence

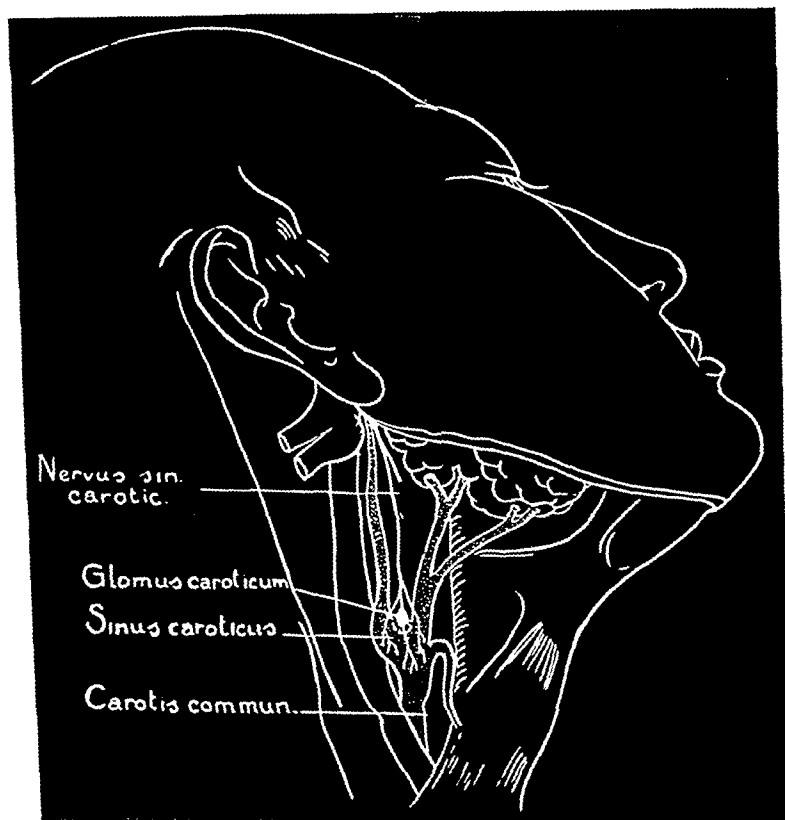


Fig. 2.—Diagram of carotid sinus in man.

of the carotid sinus mechanism by which the carotid blood pressure controls reflexly the general arterial pressure.

The term "carotid sinus" signifies a specially innervated area of the bifurcation of the common carotid artery (Figs. 1 and 2). Within this area are the origins of the internal and external carotid and the occipital arteries, the carotid bulb (which is a bulbous dilatation at the root of the internal carotid), and the carotid body or carotid ganglion which lies between the bifurcating arteries. This region is connected with the central nervous system by means of a distinct group of nerve fibers constituting the carotid sinus nerves. The nerve fibers originate in the ad-

ventitial coat of the arteries of the carotid bifurcation, mainly in the carotid bulb, and in the endothelial lining of the vessels of the carotid ganglion, as shown chiefly by De Castro<sup>18</sup> and Nonidez.<sup>19</sup>

According to a technique (Fig. 3) developed in our laboratory, one or both carotid sinuses of a dog are isolated in situ from the circulation, taking care not to injure their innervation. Such isolated sinuses then are really segments of vessels with intact nerve supply and these segments may be perfused either by means of another dog or with a Dale-Schuster perfusing pump. In this manner the pressure within the lumen of this specialized and isolated segment of the vascular tree may be raised or lowered. Since this segment is connected to the animal only

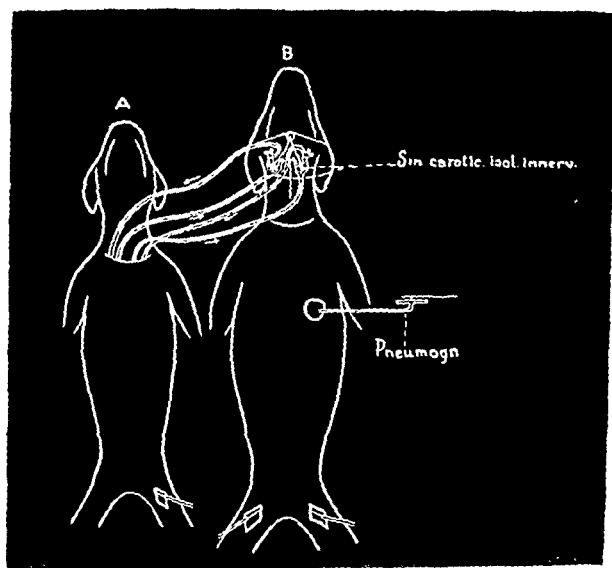


Fig. 3.—Technique of establishing isolated, innervated carotid sinuses in Dog B perfused by Dog A.

by intact nerves, it can be shown that it is only by reflexes originating within this area, due to differences in pressure, that the general blood pressure is regulated.

If the pressure inside the circulatory isolated but innervated carotid sinuses is increased, one observes (Fig. 4) that this rise of intracarotid sinus pressure is associated with a fall of the blood pressure in the general circulation of the dog. Together with the fall of arterial pressure, there is a slowing of the heart. Conversely, if the pressure is lowered in the isolated carotid sinus, the general blood pressure of the dog rises and the heart accelerates.

These experimental observations thus demonstrate that the general arterial blood pressure is automatically controlled by means of the endovascular pressure itself acting on the pressosensitive nerve endings of

the carotid sinuses. The pressosensitivity of the carotid sinus is very great; it has indeed been shown by Koch<sup>20</sup> and by my co-workers and myself<sup>5</sup> that, in the carotid sinus of the dog, an increase or a decrease of even 1 mm. mercury pressure from the normal arterial pressure is sufficient to produce reflex compensatory changes in the general blood pressure. Moreover, Bronk and Stella<sup>21</sup> could register action potential variations from the carotid sinus pressoreceptors with each systolic-diastolic variation of carotid sinus pressure.

Let us analyze briefly the components of these proprioceptive mechanisms of blood pressure regulation by the aortic and especially the carotid sinus pressoreceptor reflexes.

The regulation of the heart rate depends mainly upon reflex changes in the vagus tone and to a slight degree upon changes in the sympathetic activity.

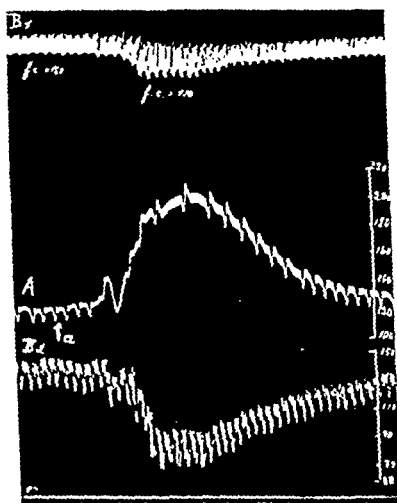


Fig. 4.—Dogs A and B prepared according to the technique shown in Fig. 3. Upper curve, heart rate of Dog B; middle curve, blood pressure of Dog A perfusing the carotid sinuses of Dog B; lower curve, femoral blood pressure of Dog E. At ↑a: adrenaline hypertension in Dog A, and hence in the carotid sinuses of Dog B, induces heart slowing and hypotension in Dog B.

The control of the circulating blood volume and the peripheral vascular resistance is mainly due to reflex changes in the arterial and venous tone and also to the changes in the tone of the arteriovenous anastomoses.

Thus, we find that an increase of carotid sinus pressure produces reflex arterial and venous dilatation and a reduction in caliber of the arteriovenous anastomoses. A lowered carotid sinus pressure produces, on the other hand, a reflex arteriolar and venous constriction and an opening of the arteriovenous anastomoses.

By means of various experimental methods, it has been shown<sup>5</sup> that these vascular reactions occur, to a certain extent, in the peripheral

ventitial coat of the arteries of the carotid bifurcation, mainly in the carotid bulb, and in the endothelial lining of the vessels of the carotid ganglion, as shown chiefly by De Castro<sup>18</sup> and Nonidez.<sup>19</sup>

According to a technique (Fig. 3) developed in our laboratory, one or both carotid sinuses of a dog are isolated in situ from the circulation, taking care not to injure their innervation. Such isolated sinuses then are really segments of vessels with intact nerve supply and these segments may be perfused either by means of another dog or with a Dale-Schuster perfusing pump. In this manner the pressure within the lumen of this specialized and isolated segment of the vascular tree may be raised or lowered. Since this segment is connected to the animal only

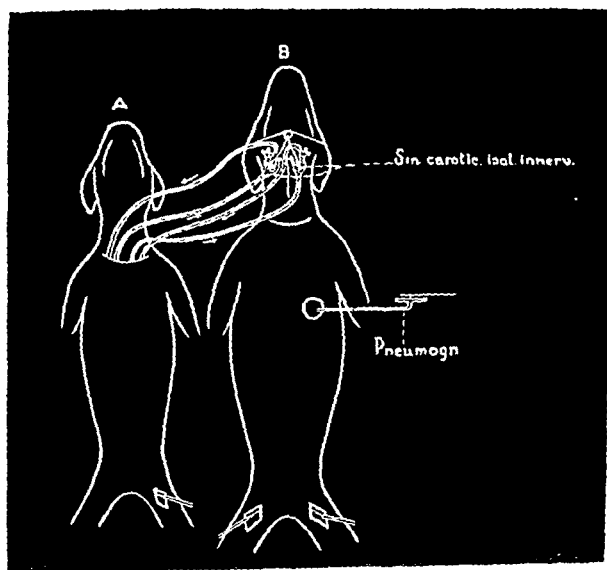


Fig. 3.—Technique of establishing isolated, innervated carotid sinuses in Dog B perfused by Dog A.

by intact nerves, it can be shown that it is only by reflexes originating within this area, due to differences in pressure, that the general blood pressure is regulated.

If the pressure inside the circulatory isolated but innervated carotid sinuses is increased, one observes (Fig. 4) that this rise of intracarotid sinuses pressure is associated with a fall of the blood pressure in the general circulation of the dog. Together with the fall of arterial pressure, there is a slowing of the heart. Conversely, if the pressure is lowered in the isolated carotid sinus, the general blood pressure of the dog rises and the heart accelerates.

These experimental observations thus demonstrate that the general arterial blood pressure is automatically controlled by means of the endovascular pressure itself acting on the pressosensitive nerve endings of

anism. Indeed, experimental observations with Bouckaert and Nowak<sup>23, 24</sup> have shown that the reflex neurovascular regulation of the blood pressure occurs quite well in the absence of the suprarenal medullary secretion. The increased discharge of adrenaline in response to lowered carotid sinus pressure is thus comparable to the increased release of adrenaline in response to emergencies, as demonstrated by Cannon.<sup>25</sup>

Finally, another group of experiments has permitted us to assert that the carotid sinus zone, as well as the cardioaortic area, is provided with a reflexogenic innervation which is not only pressosensitive but also chemosensitive, so that changes in oxygen or carbon dioxide content in the blood and also the presence of several pharmacologic sub-

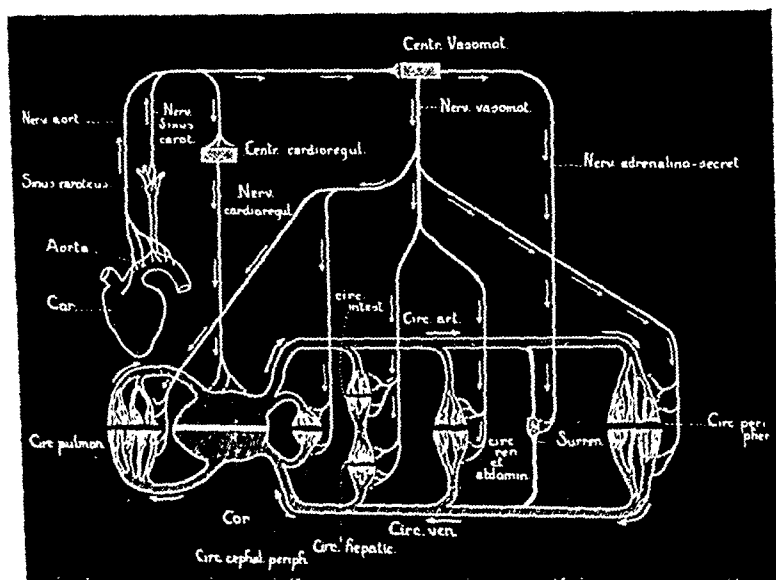


FIG. 6.—Diagram of the circulation and of the reflex neurovascular, neurocardiac, and adrenaline regulation of heart rate, vascular tone, and blood pressure by means of the cardioaortic and carotid sinus presso- and chemoreceptive mechanisms.

stances in the arterial blood can influence, by means of carotid sinus and aortic reflexes, the activity of the cardiovascular centers and thus modify the general blood pressure. These chemoreceptors of the carotid sinus are localized (Fig. 5) in the glomus caroticum, annexed to the carotid bifurcation, and are quite different from the pressoreceptors.

Fig. 6 shows schematically the afferent and efferent pathways of the proprioceptive mechanisms of cardiovascular regulation by means of the carotid sinus and cardioaortic presso- and chemosensitive areas.

Another question presents itself at this point: Are the cardioaortic and carotid sinus vascular zones the only regions provided with reflexogenic pressosensitivity and able to take part in the proprioceptive regulation of heart rate, vascular tone, and blood pressure?



vessels, but take place mostly in the splanchnic area; that is to say, the mesenteric vessels, the spleen, liver, intestines, and kidneys.

Concerning the reflex regulation of the venous vascular tone by the carotid sinus pressoreceptive reflexes, the investigations of Fleisch<sup>22</sup> and myself with Bouckaert, and Regniers<sup>23</sup> show that the mesenteric veins, isolated from general circulation but perfused in situ by means of Donegan's technique, contract reflexly in response to a lowering of carotid sinus pressure and dilate if the sinus pressure is increased. Thus, both the tone and the capacity of the abdominal venous reservoirs are controlled reflexly and automatically by the arterial blood pressure acting on the pressosensitive carotid sinus nerve endings.

The arteriolar and venous vascular tones are regulated not only by the carotid sinus and aortic reflexes by means of neurovascular influ-

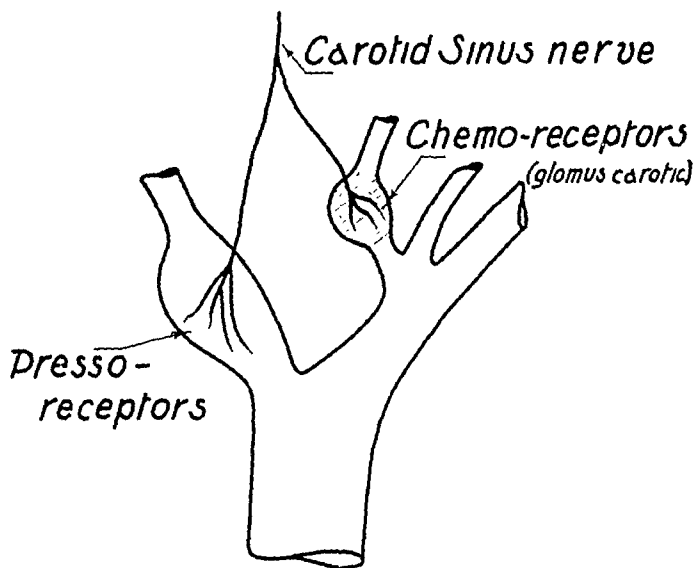


Fig. 5.—Diagram of the presso- and chemoreceptors of carotid sinus.

ences, but also by reflex alterations in the adrenaline output. Our experiments<sup>4, 5</sup> showed indeed that, when the pressure rises in the carotid sinus, the adrenaline discharge of the suprarenals is reflexly reduced; when the carotid sinus pressure is lowered, more adrenaline is liberated by the suprarenals.

Therefore, the arterial blood pressure, by acting on the pressoreceptors of the carotid sinus, provides one of the mechanisms for regulating the secretion and discharge of adrenaline, and thus further controls, in a humoral manner, the vascular tone, the heart rate, the circulatory blood volume, and probably also the caliber of the arteriovenous anastomoses.

I wish to point out that this suprarenal hormonal regulation of the circulation by the carotid sinus is only an accessory regulating mech-

Fig. 7 shows schematically the main functions of the pressosensitive reflexogenic vascular areas in the proprioceptive cardiovascular regulation.

After this review of the proprioceptive mechanisms of the regulation of general blood pressure, I propose to examine the significance of these mechanisms in the pathology of chronic arterial hypertension.

The cardioaortic and carotid sinus nerves not only are the means of the automatic pressoreceptive reflex regulation of general arterial pressure but also are the *buffer or moderator nerves* of the blood pressure.<sup>5, 17, 20</sup> In fact, functional suppression of the aortic and carotid sinus nerves produces immediately an intense arterial hypertension; in dogs the pressure may rise from 130 to 250 to 300 as a consequence of the section of the aortic and carotid sinus nerves (Fig. 8 I). This marked increase of blood pressure is due to the release of vasoconstrictor and cardioaccelerator centers, the activity of which, under normal condi-

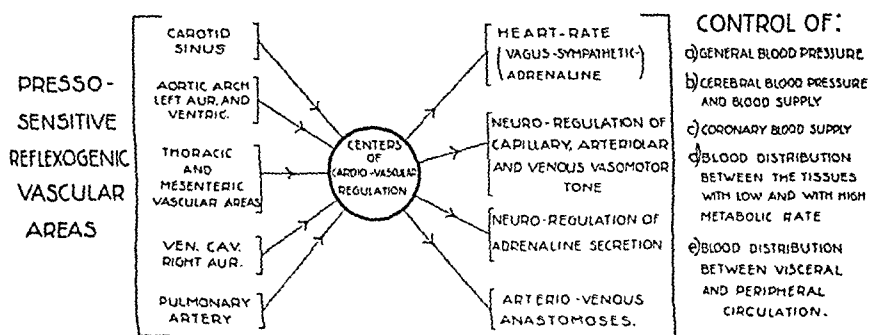


Fig. 7.—Diagram of the functions of the pressosensitive reflexogenic vascular areas in the proprioceptive cardiovascular regulation.

tions, is permanently moderated reflexly by the aortic and carotid sinus nerves. The moderator tone of these nerves is maintained and regulated by means of the pressure and the chemical constitution of the blood acting on the presso- and chemosensitive nerve endings of the cardioaortic and carotid sinus vascular areas.<sup>5</sup>

In dogs my co-workers and I<sup>5, 22</sup> have observed arterial hypertension maintained at 250 to 300 for periods of nine to twenty-six months after section of the cardioaortic and carotid sinus moderator nerves (Fig. 9). The same observation has been made by Nowak<sup>23</sup> on dogs up to three years after section of these moderator nerves. If, in a certain number of animals, section of the cardioaortic and carotid sinus nerves produces only a temporary hypertension, this is due to the presence of accessory fibers of the cardioaortic nerves in the vagus, or because in certain animals the pulmonary and mesenteric intestinal pressosensitive nerves may take over the moderator function of the cardioaortic and carotid sinus nerves.

Experimental observations by Bainbridge<sup>26</sup> and by McDowall<sup>27</sup> have shown that the right auricle, as well as the venae cavae at their entrance into the heart, are provided with receptors through which pressure changes in the venous system influence reflexly the heart rate and the arterial vascular tone.

More recently Schwiegk<sup>28</sup> showed that the branches of the pulmonary artery also are endowed with reflexogenic pressosensitivity regulating the heart rate and arterial vasomotor tone. Increase of pressure in the pulmonary arterial system causes reflex heart slowing and arterial vasodilatation, while lowering of pulmonary arterial pressure provokes the opposite cardiovascular reactions.

The centripetal pathways from these venoauricular and pulmonary arterial pressoreceptors are found in the cervical vagus nerves.

In 1929 we observed,<sup>4</sup> however, that experimental suppression of the cardioaortic, carotid sinus, and cervical vagus nerves did not abolish completely the proprioceptive mechanism of cardiovascular regulation. Indeed, in a dog deprived of the pressosensitive reflexogenic innervation of the cardioaortic, carotid sinus, venoauricular, and pulmonary zones, the elevation of general arterial pressure still induced compensatory reactions characterized by vascular dilatation and diminution of adrenaline output. In the same animal arterial hypotension started the opposite compensatory reactions of vascular constriction and increased adrenaline secretion. This proprioceptive adaptation and control of vasomotor tone by the blood pressure is not of direct central origin. These reactions still persist in the "spinal" animal.

Experiments employing several different methods have permitted us, with the collaboration of Bouckaert, Farber, Hsu, and Wierzechowski,<sup>29, 30</sup> to show that, in the dog deprived of carotid sinus, cardioaortic, pulmonary, and venous pressosensitive zones, as in the spinal animal, the proprioceptive regulation of vascular tone occurs through pressosensitive reflexes originating mostly from the vascular territory of the celiac and mesenteric arteries, and secondly from the territory of the thoracic arteries. These vasomotor reflex responses to blood pressure variations may arise in part from the mesenteric pressoreceptors located in the Pacinian mesenteric corpuseles, as shown by Gammon and Bronk,<sup>31</sup> who recently registered centripetal action currents, related to blood pressure changes, from these organs.

These experiments raise another question: Are all vessels provided with reflexogenic pressosensitivity? There are experimental facts which make it possible to answer in the negative. Proprioceptive regulation of general vascular tonus is effected through reflexes, the pressoreceptors of which are situated only in certain well-localized vascular areas; namely, the carotid sinus, cardioaortic, venoauricular, pulmonary arterial, and thoracicosplanchnic zones.

moregulation, the psychic and motor behavior of these totally sympathetomized dogs were, however, normal as also shown by Samaan,<sup>35</sup> Brouha, Cannon, and Dill.<sup>36</sup> After each operative stage of the sympathetomy, the animal passes, of course, through a period of one or two weeks of general depression; the blood pressure is lowered as a consequence of the removal of an important part of the vasomotor tone of central origin. Soon, a progressive rise in peripheral vascular resistance is restored by means of a vasopressor mechanism, originating, in part, in the sympathetic synapses located more peripheral to the paravertebral chains, and in the vascular wall. Thus the general blood pressure returns to normal levels. At complete rest, the blood pressure of the totally sympathetomized dog, however, may be somewhat under the mean level of normal dogs as a consequence of the slow rate of the heart deprived of its sympathetic innervation and controlled only by the vagal cardioinhibitory tone.

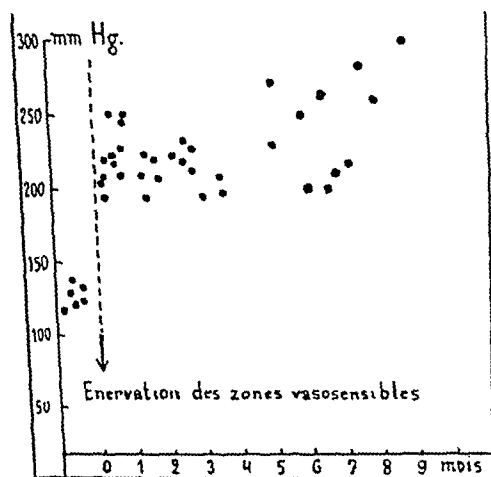


FIG. 9.—Blood pressure of six dogs before and after section of the four moderator nerves.

The question arises: Is the experimental hypertension induced by exclusion of the moderator nerves related to permanent clinical hypertension? We can, at least, answer a part of this question in the negative. This form of experimental hypertension varies from the typical nephropathic variety, but resembles more closely the so-called "essential neurogenic hypertension." This suggests that a functional deficiency of the moderator nerves, either in the region of the vasoconstrictor centers, in the region of the peripheral pressoreceptors, or in the region of the peripheral vasoconstrictor nerves, could be the underlying cause for essential hypertension and that surgical interruption of the efferent vasopressor sympathetic nerve paths might be indicated in this condition of "neurogenic" hypertension.

The degree of hypertension which develops after section of the moderator nerves depends mainly upon the sympathetic vasopressor tonus. This tonus is an index of the state of activity in the cortical psychomotor, hypothalamic, and bulbar centers, as well as the result of a series of humoral and cellular factors among which are the blood supply to the sympathetic centers and the  $\text{CO}_2$  and oxygen content of the blood.

With Bacq, Brouha, and Bouckaert, I<sup>32, 34</sup> could show, indeed, the role of the vasopressor sympathetics in the mechanism of experimental hypertension produced by exclusion of the moderator nerves.

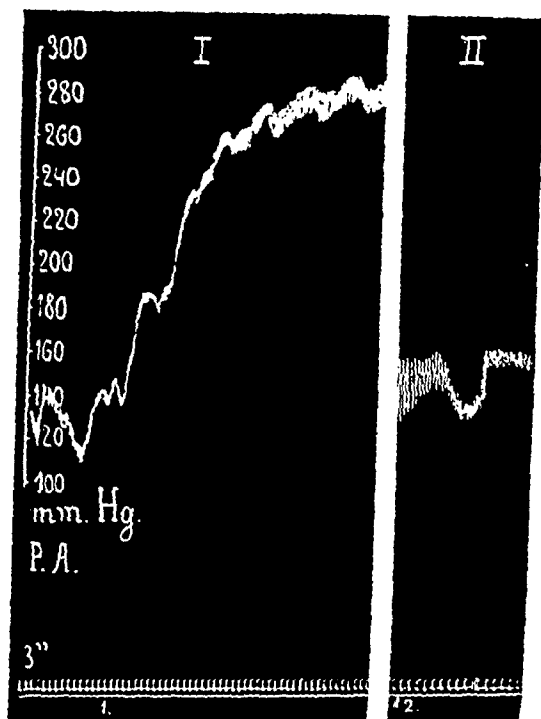


Fig. 8.—*I*, blood pressure of a normal dog; at 1, section of the four moderator nerves; hypertension. *II*, blood pressure of a totally sympathectomized dog; at 2, section of the four moderator nerves; no hypertension.

In dogs total excision of the sympathetic paravertebral ganglionic chains, from the stellate ganglia down to the pelvic ganglion, performed in three operative stages, prevents (Fig. 8 *II*) or causes the disappearance of this type of experimental hypertension. We noticed also that the pressoreceptive reflexes of cardioaortic and carotid sinus origin, regulating vascular tone and arterial pressure, are absent in the totally sympathectomized dog. No vasomotor response could be detected either by reflex or direct stimulation of the vasomotor centers in dogs up to several months and for as long as one year after total removal of the sympathetic chains. The general arterial pressure (Fig. 8 *II*), the ther-

moregulation, the psychic and motor behavior of these totally sympathectomized dogs were, however, normal as also shown by Samaan,<sup>35</sup> Brouha, Cannon, and Dill.<sup>36</sup> After each operative stage of the sympathetomy, the animal passes, of course, through a period of one or two weeks of general depression; the blood pressure is lowered as a consequence of the removal of an important part of the vasomotor tone of central origin. Soon, a progressive rise in peripheral vascular resistance is restored by means of a vasopressor mechanism, originating, in part, in the sympathetic synapses located more peripheral to the paravertebral chains, and in the vascular wall. Thus the general blood pressure returns to normal levels. At complete rest, the blood pressure of the totally sympathectomized dog, however, may be somewhat under the mean level of normal dogs as a consequence of the slow rate of the heart deprived of its sympathetic innervation and controlled only by the vagal cardioinhibitory tone.

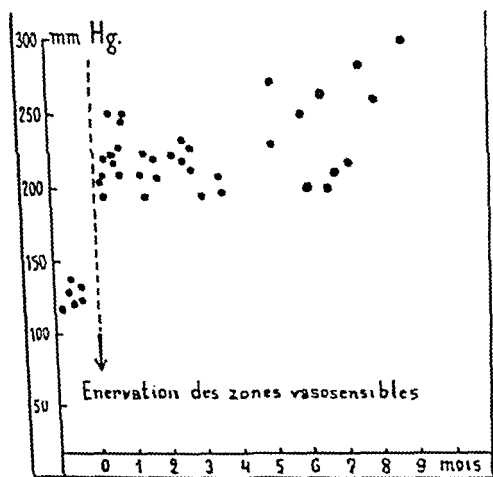


Fig. 2.—Blood pressure of six dogs before and after section of the four moderator nerves.

The question arises: Is the experimental hypertension induced by exclusion of the moderator nerves related to permanent clinical hypertension? We can, at least, answer a part of this question in the negative. This form of experimental hypertension varies from the typical nephropathic variety, but resembles more closely the so-called "essential neurogenic hypertension." This suggests that a functional deficiency of the moderator nerves, either in the region of the vasoconstrictor centers, in the region of the peripheral pressoreceptors, or in the region of the peripheral vasoconstrictor nerves, could be the underlying cause for essential hypertension and that surgical interruption of the efferent vasopressor sympathetic nerve paths might be indicated in this condition of "neurogenic" hypertension.

Recently, Allen and Adson<sup>37</sup> concluded from their clinical observations that bilateral resection of the splanchnic nerves, celiac ganglion, and two upper lumbar sympathetic ganglions, for essential hypertension, can be carried out without undue risk, that patients are not disabled as a result of this operation, and that the blood pressure of many of them is significantly reduced. Other patients note amelioration or relief of symptoms even when their blood pressures have not been significantly reduced.

A second method which will produce experimental hypertension was described by Dixon and Heller.<sup>38</sup> These authors injected a kaolin suspension into the cerebral ventricles or into the subarachnoid space. The mechanical compression, produced by the kaolin, led to cerebral anoxemia which particularly sensitizes the vasopressor centers to the stimulating action of CO<sub>2</sub>. That anemia and anoxemia may stimulate the vasopressor centers has been demonstrated by several experimenters. Raab<sup>39</sup> has shown, in the laboratory of Cannon, that central anemia, especially central acidosis, stimulates the vasopressor centers and increases their sensitivity to the humoral CO<sub>2</sub>. In our laboratory, Nowak and Samaan,<sup>40</sup> by perfusing the isolated head connected to the trunk only by the spinal vasomotor pathways, also produced evidence that acute anemia alone in the cerebral circulation provokes an intense somatic arterial hypertension. Experiments of Nowak<sup>41</sup> further observed that the permanent decrease of cerebral blood supply by ligature of the carotid arteries, vertebral and spinal arteries may induce, in dogs, a condition of permanent arterial hypertension. These experimental observations support the views of Kylin<sup>42</sup> and Raab,<sup>43</sup> who believe that some forms of clinical hypertension are related to some process of anoxic nature, such as endarteritis, localized in the region of the vasopressor centers.

Recently Goldblatt and co-workers<sup>44</sup> made a very important observation. They showed that, in the dog and in the monkey, renal ischemia by permanent incomplete compression of the renal arteries caused chronic, progressive arterial hypertension, with elevation of both the systolic and the diastolic pressures. This fact has largely been confirmed by Page<sup>45</sup> and others and in our laboratory by Elaut,<sup>46</sup> Bouckaert, and myself.<sup>47</sup> In our experiments we obtained permanent hypertension in dogs reaching 245. Furthermore, we observed<sup>47</sup> that the carotid sinus vasopressor and hypertensive reflexes were especially active in such hypertensive dogs. Page<sup>45</sup> and Collins<sup>48</sup> observed that in dogs excision of the extrinsic renal nerves alone does not prevent experimental hypertension due to renal ischemia. The experiments of Goldblatt and his collaborators<sup>49</sup> showed that neither excision of one suprarenal body with denervation and destruction of the medulla of the other suprarenal, nor excision of the splanchnic nerves and the lower dorsal ganglia, which constitute an

important part of the sympathetic vasopressor system, prevents or cures experimental hypertension produced by renal ischemia.

More recently experiments performed by Bayless, Bouckaert, Elaut, and Samaan, and myself,<sup>50</sup> showed that complete excision of the whole sympathetic ganglionic chains in dogs also does not prevent the arterial hypertension following renal ischemia. The same observations have been made by Freeman and Page,<sup>51</sup> and Alpert, Alving, and Grimson.<sup>52</sup>

Our experiments<sup>47, 50</sup> suggest that the arterial hypertension induced by renal ischemia may be due to an humoral factor which increases the excitability of the peripheral blood vessels to constrictor stimulations, mainly to the neurogenic vasoconstrictor influences; the same humoral factor inducing, on the other hand, a direct peripheral vasoconstriction and a disturbance in the physiologic mechanisms of the pressoreceptive reflex regulation of blood pressure. The sympathectomy up to the total removal of both ganglionic chains neither prevents nor cures this experi-

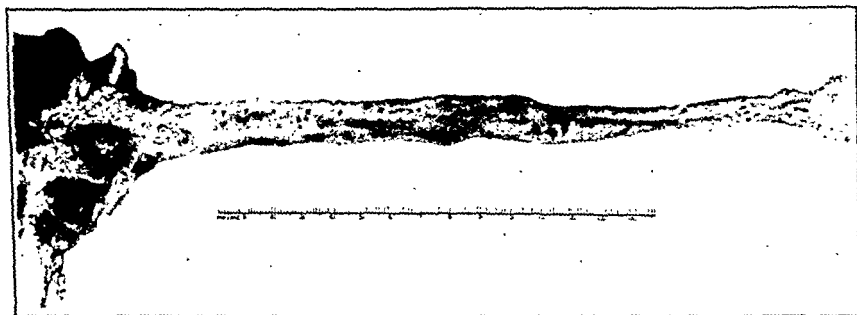


Fig. 10.—Lesions in the aorta of a thyroidectomized dog treated with large doses of vitamin D<sub>2</sub>.

mental nephrogenic hypertension. But, as pointed out by Goldblatt, although the results of these investigations are in agreement with the conclusions of Prinzmetal and Wilson<sup>53</sup> and of Pickering<sup>54</sup> concerning the part played by the vasomotor system in human hypertension of nephropathic origin, yet they do not necessarily exclude some beneficial effects of operations on the vasomotor system or on the suprarenal glands in some cases of nephropathic hypertension. But we agree that further experimental and clinical studies are necessary to evaluate adequately the indications and the results of these surgical interventions.

A fourth method of producing experimental arterial hypertension is that indicated by Appelrot.<sup>55</sup> Further researches along this line were carried out by Handovsky<sup>56</sup> in this laboratory with the collaboration of Goormaghtigh,<sup>56</sup> of the Department of Pathology.

Their studies show that the repeated administration of relatively large doses of vitamin D<sub>2</sub> (calciferol) to dogs provoked a progressive augmentation of the arterial blood pressure. It was noticed also that the experimental dogs were very sensitive to the hypertensive action of adrenaline.



In the kidneys and elsewhere certain vascular lesions, mainly arteriolo-neerosis, developed which could be almost superimposed upon those found in human eclampsia, diphtheria, and scarlet fever. It is furthermore interesting to mention that vitamin D<sub>2</sub>, which provokes arteriosclerosis in the rat and rabbit, does not induce the same vascular changes in the dog, unless one deprives this animal of its thyroid gland. Thus, in the thyroidectomized dog the administration of vitamin D<sub>2</sub> provokes arterial hypertension and with it intense and unusual vascular changes in the aorta and its major branches (Fig. 10), and typical lesions in the smaller arteries. We believe that these observations are interesting, since this form of experimental hypertension, characterized by high pressure and vascular lesions and sclerosis, resembles some types of human hypertension. As a matter of fact, many pathologists (Rössle,<sup>57</sup> Wegelin,<sup>58</sup> Behr,<sup>59</sup> Schmidtman<sup>60</sup>) and clinicians have referred to a relationship between the thyroid gland, arteriosclerosis, and hypertension. The researches of Aub and his collaborators<sup>61</sup> showed especially the close relationship between the thyroid and calcium metabolism.

These different groups of investigations surveyed in this lecture show once more the bonds closely uniting experimental physiology, pathology, and surgery in attempts to elucidate the mechanisms regulating arterial blood pressure and the causes of hypertension. The knowledge thus gained, it is hoped, will lead to a more adequate treatment of this very important disease.

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# ESSENTIAL HYPERTENSION: THE SELECTION OF CASES AND RESULTS OBTAINED BY SUBDIAPHRAGMATIC EXTENSIVE SYMPATHECTOMY\*

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**H**YPERTENSION, or persistent elevation of the blood pressure, may produce progressively severe symptoms and in spite of all types of treatment it may terminate fatally. In addition to the medical measures used in treating the more serious types of hypertension, operations upon the sympathetic nervous system have been devised and carried out in a large number of cases; the mortality has been low and the results have been gratifying. However, at the Mayo Clinic we have been impressed with the importance of the selection of cases suitable for operation. Subdiaphragmatic extensive sympathectomy has been performed in 158 cases in the Section on Neurosurgery at the Mayo Clinic. There has not been an operative death and there were only five deaths after operation. Following the operation, the clinical improvement varied with the progress of the disease, the age of the patient, and the amount of vascular, cardiac, and renal damage. To determine the amount of potential physiologic response obtainable following sympathetic denervation, certain tests have been devised (Table I). These tests have prevented unsuccessful operations and have indicated in which cases a satisfactory lowering of the blood pressure or relief of clinical symptoms may be expected to occur after the operation.

TABLE I  
PREOPERATIVE TESTS FOR HYPERTENSION

- 
- |                                                                     |
|---------------------------------------------------------------------|
| 1. Effect of rest and sleep for 24 hours                            |
| 2. Effect of 3 gr. sodium amytal each hour for 3 doses              |
| 3. Effect of $\frac{1}{2}$ gr. sodium nitrite each hour for 6 doses |
| 4. Effect of 5% pentothal sodium intravenously                      |
- 

In essential hypertension there is increased peripheral arterial resistance, which is attributable to abnormal response of the arterioles to certain stimuli that produce marked fluctuation in blood pressure, emotion or cold increasing it greatly. There is some evidence that there are no abnormal vasomotor stimuli in essential hypertension; hence, it must be assumed that the arterioles react excessively to normal vasomotor stimuli.

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Postoperative observations have shown that, when the blood pressure fluctuates widely and reaches low levels at times, operation (that is, interruption of vasomotor impulses) is most beneficial, but, when the blood pressure is fixed at high levels, surgical treatment is ordinarily of little value. This emphasizes the necessity of preoperative tests to determine the flexibility of the blood pressure.

For convenience, essential hypertension has been divided into four clinical groups: Group 1 consists of cases in which there are mild sclerosis of the retinal arteries and a slight increase in blood pressure, which ordinarily becomes normal as a result of rest. In Group 2 have been placed cases in which there are moderate to severe hypertension, moderate sclerosis of the retinal arteries, and occasionally venous thrombosis and arteriosclerotic retinitis. Group 3 includes cases in which there is moderate to severe hypertension associated with a definite angiospastic retinitis. The severe and advanced types of the disease are included in Group 4; in the cases in this group there is very severe hypertension that is associated with an angiospastic retinitis and edema of the optic disks. This classification may be unsatisfactory because it fails to indicate the importance of the rapidity of progression. As a working basis, however, the classification is acceptable, since the seriousness of hypertension ordinarily increases progressively as the number of the group into which it is classified increases.

The medical treatment of mild essential hypertension is usually satisfactory but severe hypertension does not respond satisfactorily to medicine and diet. Some patients who have moderate hypertension Group 2 or 3 respond rather well to medical treatment; however, a non-toxic, adequate and prolonged vasodilator would solve the problem of the treatment in many cases. Unfortunately, no such substance is available. The nitrites, acetylcholine and acetyl-beta-methylcholine have in common a vasodilating action which is too short to be very valuable. Bismuth subnitrate, when administered orally, is of little value. There is some evidence that potassium thiocyanate may be effective (both before and after operation), but the dosage must be carefully regulated. The sedatives, particularly the barbiturates, are the most valuable drugs. The amount of sedative drug which should be given three or four times a day should be great enough to abolish nervousness and restlessness and small enough to avoid drowsiness and excessively slowed mental reactions. Many patients suffering from essential hypertension do not respond adequately to medical treatment. Surgical treatment is being advised only in these cases.

The purpose of surgical treatment of essential hypertension is to produce prolonged vasodilatation by interrupting the vasoconstrictor nerves to certain parts of the arterial system. Among the earliest operations employed were bilateral lumbar sympathetic ganglionectomy and cervicothoracic sympathetic ganglionectomy. These procedures were

not effective in lowering the blood pressure for a prolonged period because the operation was limited in its scope in that it did not denervate a sufficient vascular area. A more extensive operation consisting of intradural section of the ventral roots of the spinal nerves from the sixth thoracic segment to the second lumbar segment interrupts the sympathetic fibers which pass through these roots and which carry vasoconstrictor impulses. The entire vascular area below the diaphragm is thus denervated; this creates a reservoir which is unaffected when the undenervated vessels go into a spasm. Also, the suprarenal glands are denervated by interrupting the sympathetic fibers before they enter the capsules of the glands. This eliminates the central influence in producing excessive secretion of epinephrine under emotional stress. A thorough denervation of renal arteries and arterioles is performed. This increases the circulation of the kidneys and aids in the elimination of metabolic products which may play some role in the production of hypertension.

Following rhizotomy, the values for both the systolic and diastolic blood pressures of some patients remained lower than they were before the operation. This relieved the symptoms of hypertension. However, laminectomy and rhizotomy involved an unwarrantable surgical risk and the section of the splanchnic nerves alone proved inadequate in relieving hypertension. Therefore, the resection of all three splanchnic nerves, with a portion of the celiac ganglion, and removal of the upper lumbar ganglions on each side through a subdiaphragmatic approach was finally adopted (Fig. 1). In a rather large series of cases resection of one-third to one-half of each suprarenal gland was done, but this procedure has been discontinued; however, the glands are palpated for the presence of a tumor. The operation is divided into two stages and an interval of ten days is allowed to elapse between the operations on the right and the left sides respectively. From our studies, the subdiaphragmatic extensive sympathectomy is larger in scope and interrupts more thoroughly the efferent fibers from the thoracolumbar sympathetic outflow than does the supradiaphragmatic operation.

The futility of carrying out extensive sympathectomy in cases of hypertension in which there is irreparable damage to the cardiovascular mechanism is apparent. The operation should not be considered in a case in which there is mild and slowly progressive disease that is amenable to medical treatment. Operation seems most efficacious in the definite vasospastic type of hypertension in which sharp and brisk rises in blood pressure occur when the hands are immersed in cold water and in cases in which a marked fall in blood pressure is produced when pentothal sodium, sodium amytal, or a nitrite is administered. As an average rule, the patient must be under 50 years of age and the hypertension must be classed as of Group 2 or 3.

The so-called cold test is carried out by determining the blood pressure while the patient is resting and by continuing the determination until the value for the blood pressure reaches a basal level. A hand is then immersed, to the wrist, in water at 4° C. for one minute, and the blood pressure is determined at the end of thirty seconds and of one minute

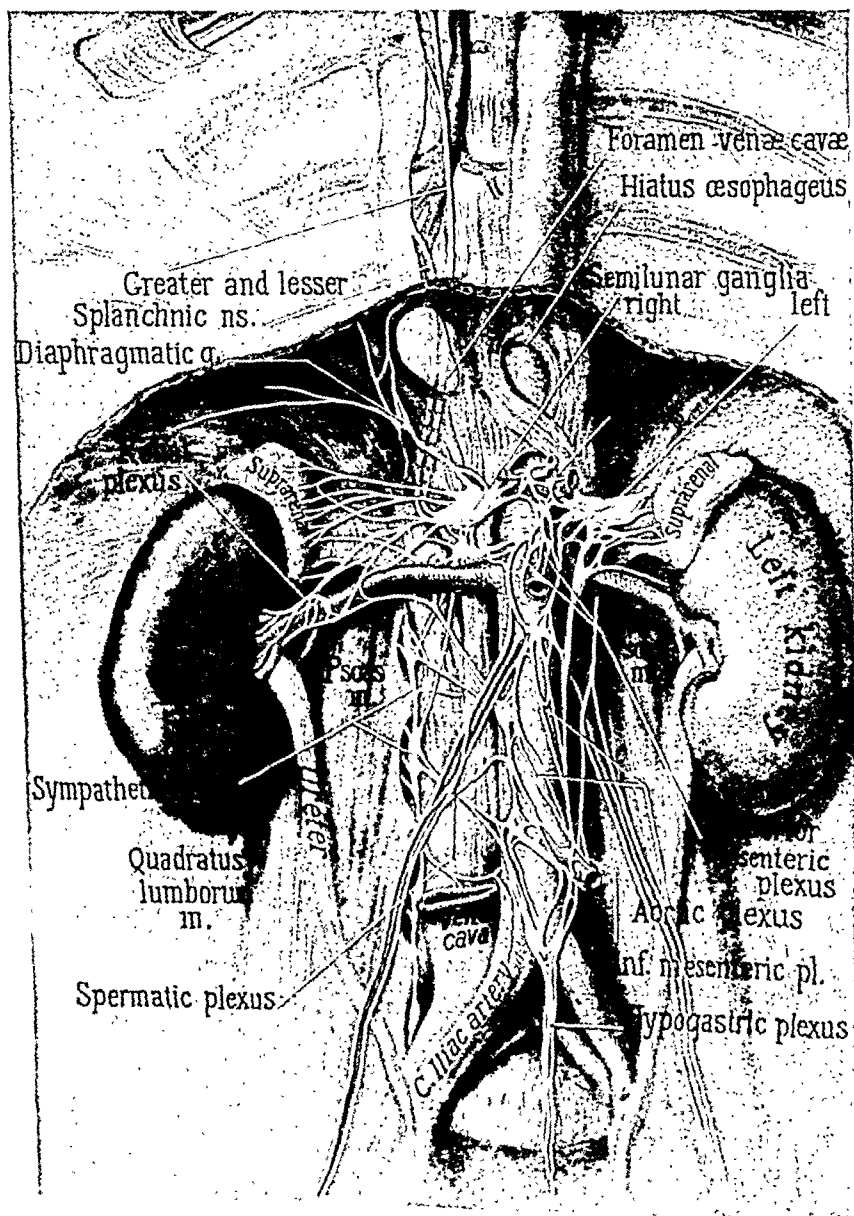


Fig. 1.—Anatomic representation of the major, minor, and lesser splanchnic nerves, celiac ganglion, upper lumbar sympathetic ganglions, and interruption of the sympathetic fibers in subdiaphragmatic extensive sympathectomy (From Labat: *Regional Anesthesia*, W. B. Saunders Company).

thereafter. The highest value is considered characteristic of the response. The response of the blood pressure to this test is a measure of the way in which it responds on innumerable occasions to such stimuli as anxiety, fright, and mental stress and strain. In cases in which operation has produced a significant decrease in blood pressure, the systolic blood pressure responds less sharply to the test than does the diastolic pressure.

The following standard tests have been adopted and operation is advised only for patients whose blood pressure responds satisfactorily preoperatively: (1) slow and intermittent intravenous injection of a 5 per cent solution of pentothal until there is no further drop in the blood pressure; ordinarily 500 mg. to 1 gm. of the drug is injected; (2) administration of 3 gr. (0.2 gm.) of sodium amytal each hour for three successive hours; (3) administration of  $\frac{1}{2}$  gr. (0.032 gm.) of sodium nitrite at intervals of thirty minutes until six doses have been given, and (4) hourly determination of blood pressure during rest and sleep for a minimum of twenty-four consecutive hours.

If the blood pressure decreases to normal or to nearly normal as a result of all these measures, the patient may be considered a satisfactory candidate for operation. If the response of the blood pressure to these measures is inadequate, the effect of operation is almost certain to be unsatisfactory. Unfortunately, even when these tests indicate that results of operation should be satisfactory, the actual results obtained will not necessarily be as good as the tests indicate. In other words, in spite of satisfactory response of the blood pressure to tests before operation it is possible that the blood pressure will not be reduced significantly by operation. At the clinic, we have made it a practice to perform the operation only in cases in which hypertension has been progressive in spite of medical supervision. However, we wish to emphasize that in almost every case of essential hypertension there is a period during which operation may be a valuable therapeutic procedure and one during which operation will almost certainly be valueless. Hence, if patients who have essential hypertension are to be operated upon, operation must be performed before the blood pressure becomes relatively fixed at high levels.

Contraindications for operation are as follows: An age of more than 50 years, congestive heart failure, angina pectoris, marked renal insufficiency, and advanced arteriosclerosis. Spasm and apparent sclerosis of the retinal arteries, retinitis, moderate enlargement of the heart, inversion of T-waves in the electrocardiogram, albuminuria, slight reduction in renal function, and a cerebrovascular accident from which recovery has been satisfactory are not in themselves considered contraindications to operation.

In carrying out extensive sympathectomy, the incision employed and the position of the patient on the operating table are similar to those employed for exploration of the kidney, except that the upper portion of the incision is extended high enough to include the oblique fibers of the latissimus dorsi muscle which will expose the twelfth rib. The incision is extended downward and outward over Petit's triangle, in order to expose the capsule of the perinephritic fat. Periosteal resection of the twelfth rib is then done; care is taken not to injure the pleura. The subcostal ligament of the twelfth rib is then incised; this allows upward retraction of the intercostal vessels and nerves and affords adequate exposure of the splanchnic nerves and lumbar ganglions. The liver is displaced forward and downward, as well as the capsule of perinephritic

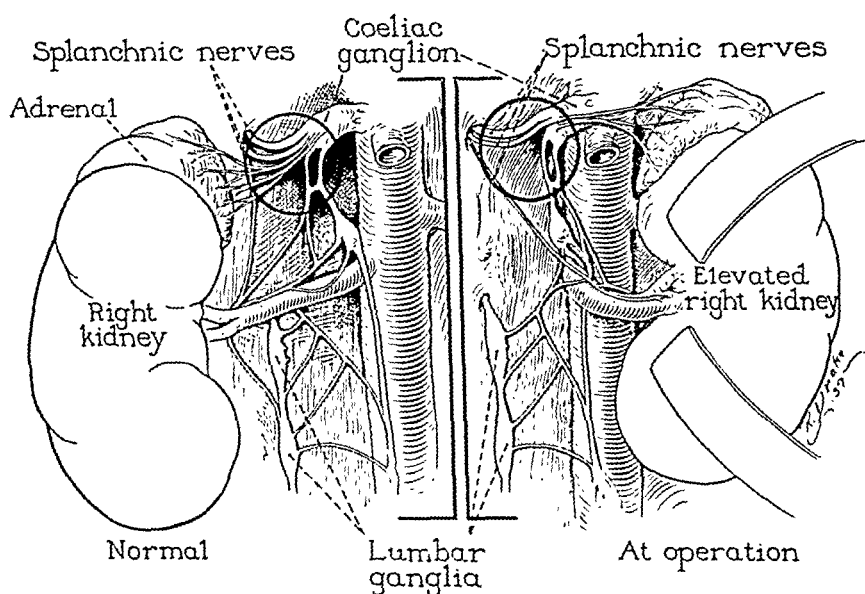


Fig. 2.—Diagrammatic representation of subdiaphragmatic sympathectomy, showing the normal relation of the ganglions and ramuli (the kidney has been retracted).

fat. At this point a laparotomy sponge that has been moistened in physiologic saline solution is inserted to protect the peritoneum and its contents, which are being dissected from the underlying muscles. Gentle dissection with moist cotton-ball sponges reveals first a splanchnic trunk which is composed of major, minor, and lesser splanchnic nerves, which are descending from above downward between the two crura of the diaphragm. They are about 2 cm. in length and end in the coeliac ganglions. The resection includes the greater portion of the ganglion and the splanchnic nerves. The first and second lumbar sympathetic ganglions are exposed along the mesial border of the psoas muscle, and they are removed with the intervening trunk in order to interrupt fibers that pass downward in the lower end of the sympathetic trunk as well



as to interrupt white rami carrying efferent impulses to the upper two sympathetic lumbar ganglions. In this manner the splanchnic vessels, the suprarenal glands, and the kidneys are denervated (Fig. 2). The muscular fascial planes are approximated with continuous and interrupted sutures of chromic catgut and the skin is closed with silk sutures.

Following splanchnic resection and removal of the lumbar ganglions, the sweating function of the feet and lower part of the legs is lost. The cutaneous temperature is definitely increased and continues to remain so permanently. There is paralysis of the ejaculatory powers and of the muscles of the urogenital trigon that is similar to that which follows neurectomy of the presacral nerves. The menstrual cycle is not altered; moreover, the reproductive functions of the female are not changed. However, sterility of the male does result, although potentia and libido fortunately are not disturbed. Although this extensive sympathectomy deprives the small and large intestine, the ureters, and the bladder of the sympathetic innervation, it does not appear to increase the frequency or urgency of micturition or of defecation. Curiously enough, the atonic intestine, the dilated colon which so frequently troubles constipated people, and Hirschsprung's disease are definitely improved by this operation, since section of the sympathetic fibers to the intestine results in decrease of the inhibitory stimuli. The same applies to the muscular mechanism of the ureters and bladder.

Two definite phenomena in the cardiovascular mechanism develop following this operation. The first is a fall in blood pressure which occurs when patients first get out of bed and stand in the erect position. The second is the development of tachycardia. The first can be relieved with a tight binder and the second can be overcome by a decrease in exertion.

The effect of operation on symptoms, while variable, is roughly proportional to the effect on the blood pressure. However, patients not infrequently note relief of headache, fatigue, pain in the thorax, "dizziness," and nervousness, in spite of the fact that the blood pressure has not been greatly reduced by operation. It is probable that some of the symptoms associated with hypertension, such as headache, may occur only when the value for the blood pressure reaches an excessively high level. Operation which may reduce blood pressure only slightly may lower it sufficiently to prevent the occurrence of some of the symptoms. In most instances in which the blood pressure has been greatly reduced by operation, headache is relieved, pain in the thorax disappears, fatigue is lessened, and the patients gain weight and generally feel greatly improved. Many of them note diminution of nervousness and of a "let down" feeling, which gratifies them. Some patients have said that they feel "entirely well" or "better than in several years." In general, about 70 per cent of the entire group of patients were benefited clinically.

Some patients whose blood pressure has been greatly reduced by operation continue to note undue fatigue, weakness, and dyspnea for weeks or months after operation. One patient whose condition was followed closely did not regain normal strength until about six months after operation. We have not been able to determine definitely that the patients who noticed these symptoms following operation are those who continue to have orthostatic hypotension, but it appears that this is so.

#### SUMMARY

The surgical treatment of hypertension, which consists of subdiaphragmatic resection of the major, minor, and lesser splanchnic nerves, celiac ganglion, and lumbar sympathetic ganglions, is associated with a small risk and is followed by satisfactory alleviation of symptoms in selected cases.

Assuming that all hypertension can be divided into four groups, depending upon the severity, Group 1 does not require surgical treatment and Group 4 is too severe and too far advanced to warrant the expectation of adequate results. Groups 2 and 3 then should be considered for operative treatment. More important than the group are the pre-operative tests which indicate the potential physiologic changes that will follow sympathetic denervation of the vascular area below the diaphragm.

The so-called cold test indicates the upper limits of the blood pressure resulting from emotion or cold. The four other tests indicate the lower limits of the blood pressure readings associated with prolonged vasodilatation, and, therefore, denote the probable values for the blood pressure following extensive sympathectomy. They are as follows: (1) Twenty-four consecutive hourly determinations of the blood pressure are made while the patient is in bed, to establish the maximal blood pressure, the minimal blood pressure, and the mean or average blood pressure. (2) Slow and intermittent intravenous injection of a 5 per cent solution of pentothal sodium is made until there is no further drop in blood pressure. (3) One-half grain (0.032 gm.) of sodium nitrite is administered at intervals of thirty minutes until six doses have been given. (4) Hourly determinations of blood pressure are made during rest and sleep for a minimum of twenty-four hours.

If the blood pressure drops to nearly normal and if the patient is less than 50 years of age, the operation should be considered.

The results in a large series of cases have been quite satisfactory. The effect of the operation is physiologic in character, and, if so considered, the results justify the procedure.

## BLOOD POTASSIUM DURING EXPERIMENTAL SHOCK\*

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**I**N MAMMALS the extracellular body fluids contain from 13 to 25 mg. potassium per 100 c.c. and in individuals under basal conditions the level in the plasma remains remarkably constant, although the basic levels for individuals of the same species may differ as much as 20 per cent. It is well known that living cells, both plant and animal, contain from seven to twenty-five times as much potassium as their surrounding media.

With manifold K differences outside and inside the cell, it seemed reasonable to postulate that experimental procedures resulting in extensive tissue destruction, trauma, or injury causing increased cell permeability should result in increased extracellular potassium. Increases in the blood would only be expected to occur if the K was released from the cells too rapidly for the potassium regulating mechanism to handle. If the extracellular body fluids are depleted, their replacement by highly potassic cellular fluids should also result in a potassium rise.

It should be noted that even with the injections of potassium salts the plasma K level cannot be altered for long in normal animals (Zwemer and Truszkowski, 1937; Truszkowski and Zwemer, 1938), and that prolonged hyperpotassemia can only be produced by repeated injections. Marked elevations are injurious to the body regardless of whether the rise is a result of potassium injected, ingested, or released from the animal's own cells (Webster and Brennan, 1927). In the present paper we have followed the blood potassium levels after extensive cell injury or fluid depletion through shock to death.

### EXPERIMENTAL PROCEDURES

Cats were used in the experiments and unless otherwise noted peripheral ear blood samples were taken for whole blood potassium analysis by the method of Truszkowski and Zwemer (1937). The red blood cells of the cat have a low potassium content and whole blood of this species is therefore a valid indicator of K changes. Parallel serum values are given in the hemorrhage experiments, in which extensive

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blood sampling would not complicate the picture. Ether anesthesia was used during the period of operative and traumatic procedures in the acute experiments, with the exception of the cases in which sodium amytal was used. Blood density was determined by the method of Barbour and Hamilton (1926). A condition of primary shock was produced within a few hours by hemorrhage, crushing of limbs, or manipulation of viscera. Slower development of the secondary shock syndrome occurred after intestinal obstruction, enterostomy, and pancreatitis.

#### RESULTS

Our impression based on thousands of potassium determinations in a number of animal species and man is that plasma potassium is remarkably constant and difficult to alter for long. The relative constancy of plasma potassium is shown in an animal in which only a small amount of tissue was damaged with no production of pain. The blood potassium was followed for a period of days, with frequent samples taken on the first day (Protocol 1).

Analysis of blood samples from an animal which remained under amytal anesthesia for thirty hours during which time eight samples of blood were taken (Protocol 2) showed no change in potassium. Under amytal the variations were less than 2 mg. per cent in either direction from the initial value. Initially and when the animal recovered, the values were somewhat higher.

In the hemorrhage experiments the values also varied little until the amount of blood removed was a large proportion of the initial estimated total.

Although one might expect that crushing of muscle and hemorrhage would be the procedures most likely to raise the plasma potassium content from endogenous sources, these animals showed K rises terminally only. This agrees with Stewart (1936) who found no plasma K rise with hemorrhage, but a marked K diuresis. He did not bleed his dogs to death. Kerr (1926) and Thaler (1935) report plasma K increase after hemorrhage. It was easier to produce shock by visceral manipulation than by trauma to the extremities and concomitantly the viscera lose their K content much more easily.

The results in individual animals are illustrated by complete protocols of the effects of fatal hemorrhage, limb trauma, and visceral manipulation as listed in Table I. Some were graphed, with information supplementary to the K determination.

Table II gives data from sixteen animals in which a condition of secondary shock occurred. The initial blood potassium, the blood potassium during shock, and the interval between these two determina-

tions are given. The number of blood samples analyzed for their potassium content and the procedure initiating the shock syndrome are given also.

In animals acutely shocked with potassium salts, the blood K rises and the onset of symptoms are abrupt as in the present acute experiments (Table I); whereas, with the prolonged moderately elevated rises obtained with repeated injections (Truszkowski and Zwemer, 1938), the symptoms resemble those of the second group of cases (Table II).

The source of the blood sample is important, as it has been found in other experiments (Zwemer and Pike, 1938) that venous bloods coming from different organs may vary markedly in their potassium content. This finding and more specific studies of nerve excitation and of anesthetics on potassium changes in shock will be dealt with elsewhere.

In the foregoing experiments the blood was not taken from vessels draining the part of injury nor the region of operative procedure. Peripheral capillary blood resembles arterial blood in so far as potassium content is concerned; therefore the increases shown may in these cases be considered as holding good for arterial blood in general.

The data here presented agree with the postulate that potassium increases may be expected after severe tissue damage or extracellular fluid depletion, but that in a normal healthy animal it is difficult to disturb the potassium regulating mechanism.

#### DISCUSSION

In explanation of shock there have been many theories, each supported by extensive experimental work. For a review we refer the reader to papers by Cannon (1923), by Blalock (1936), by Meek (1936), and by Henderson (1938).

Diminished blood volume has been considered particularly important. The diminished effective blood volume might be due to fluid and electrolyte loss from the body as a whole, to capillary stasis and trapping of large amounts of blood in splanchnic or the traumatized area vascular

TABLE I  
LIST OF PROTOCOLS

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1. No. 3701.—Mild trauma, no shock, no K change
2. No. 3643.—Prolonged sodium amytal narcosis
3. No. 3701.—Arterial blood loss
4. No. 3707.—Repeated withdrawal of heart blood
5. No. 3752.—Repeated withdrawal of heart blood
6. No. 3755.—Repeated withdrawal of heart blood
7. No. 3641.—Mild trauma under sodium amytal anesthesia
8. No. 3644.—Trauma under amytal
9. No. 3640.—Severe trauma under amytal
10. No. 3650.—Severe trauma under ether
11. No. 3702.—Manipulation of viscera under ether
12. No. 3706.—Manipulation of viscera under ether with adrenals tied off

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TABLE I (CONT'D)

PERIPHERAL WHOLE BLOOD K OF THE CAT MAY REMAIN QUITE CONSTANT  
NERVE BLOCKED AND TESTES CRUSHED UNDER ETHER ANESTHESIA (NO SHOCK)

*Cat 3701*

Jan. 11, 1937	
12:30 P.M.	26.3 mg. % K
1:45 P.M.	Operation
1:55 P.M.	27.5 mg. % K
2:00 P.M.	25.6 mg. % K
3:00 P.M.	26.3 mg. % K
4:00 P.M.	25.0 mg. % K
5:00 P.M.	25.8 mg. % K
8:20 P.M.	24.8 mg. % K
Jan. 13, 1937	Testes swollen
	29.2 mg. % K
Jan. 16, 1937	26.4 mg. % K
Jan. 19, 1937	24.4 mg. % K
Jan. 21, 1937	23.8 mg. % K

EFFECTS OF PROLONGED SODIUM AMYTAL NARCOSIS

*Control Cat 3643, Weight, 2.6194 Kg.*

*Sex: female*

TIME	RELATIVE TIME	AMOUNT OF AMYTAL AD- MINISTERED	CAPILLARY BLOOD K AS MG. %	REMARKS
Oct. 22, 1936				
A.M.				
10:50	0	—	33.2	Healthy, adult cat not fasting
10:51		2.6 ml.		
11:05	15 min.	0.4 ml.		
11:15	25 min.	0.5 ml.		
11:25	35 min.			Heart rate 210; res- pirations, 42; tem- perature, 100.4
11:30	40 min.		27.2	
11:42	52 min.		29.0	Heart rate, 170; res- pirations, 33; tem- perature, 99.2; still unconscious; moves around a little
P.M.				
1:47	2 hr. 57 min.		27.1	
2:00		2.5 ml.		
2:45	3 hr. 55 min.		25.6	
4:15	5 hr. 25 min.		25.6	Has been in coma since morning; pec- uliar trembling con- dition
Oct. 23, 1936				
P.M.				
1:00	20 hr. 10 min.		27.3	Unable to move; fibrillar twitchings; drank some water after taking blood sample
Oct. 24, 1936				
A.M.				
9:30	46 hr. 40 min.		30.0	Recovered

TABLE I (CONT'D)  
EFFECTS OF ARTERIAL BLOOD LOSS

Cat 3701. Weight 3.94 Kg.

Sex: Male

Feb. 15, 1937

TIME	RELATIVE TIME	AMOUNT REMOVED	WHOLE BLOOD K MG. %	SERUM POTAS- SIUM MG. %	SERUM CA MG. %	SPECIFIC GRAVITY WHOLE BLOOD	SERUM SP. GR.	SERUM PROTEIN GM. %
Under light ether anesthesia femoral artery exposed for bleeding								
A.M.								
11:20	0	10 c.c.	—	15.4	12.9	1.0518	1.0292	7.62
11:35	15 min.	10 c.c.	21.7	16.0	12.6	1.0518	1.0289	7.52
11:45	25 min.	10 c.c.	23.0	15.3		1.0494	1.0283	7.3
11:55	35 min.	10 c.c.	21.9	14.4	11.9	1.0486	1.0278	7.13
P.M.								
12:07	47 min.	10 c.c.	22.7	15.1	11.4	—	1.0273	6.96
12:20	1 hr.	10 c.c.	21.3	13.9	11.0	1.0451	1.0251	6.2
12:30	1 hr.							
	10 min.	10 c.c.	23.1	17.1	10.8	1.0440	1.0255	6.33
12:40	1 hr.							
	20 min.	4 c.c.*	—	21.5	—	—	1.0266	6.72
Heart's blood								
12:55	1 hr.	10 c.c.	55.6	40.5	12.7	1.0452	1.0280	7.2
	35 min.							
1:00	1 hr.							
	40 min.							
			Portal vein blood.—57.8 mg. %					
			Pericardial fluid.—41.2 mg. %					

\*Blood did not flow well from artery, because of very low pressure.

REPEATED WITHDRAWAL OF HEART BLOOD\*

Cat 3707. Weight: 2.665 Kg.

Sex: Male

Anesthesia: none

Jan. 21, 1937

TIME	AMOUNT REMOVED	WHOLE BLOOD K MG. %	SERUM K MG. %	SERUM SPECIFIC GRAVITY	SERUM PROTEIN GM. %	REMARKS
Jan. 20		28.8(c)†				Fasting, healthy, adult cat
7:20						Tied on board for experiment
Jan. 21						
12:20			—	1.0293	7.6	
12:30	10 c.c.	26.8		1.0284	7.3	
12:45	10 c.c.	26.4	22.2	1.0266	6.7	
1:05	16 c.c.	—	25.3	1.0268	6.8	Air hunger
1:15	14 c.c.	29.4	25.3	1.0269	6.8	
1:30	16 c.c.	32.3	25.3	1.0254	6.3	Nictitating mem- brane out
1:50	10 c.c.	26.7	20.4			Extremities cold
2:05	10 c.c.	—	28.1	1.0265	6.6	Convulsion
2:25						Very weak; gasp- ing for air
2:26	10 c.c.	57.4	41.7			Dead
2:30						
	Total					
	96 c.c.					

\*Calculated original blood volume: 160 c.c.

†(c)—Capillary blood.

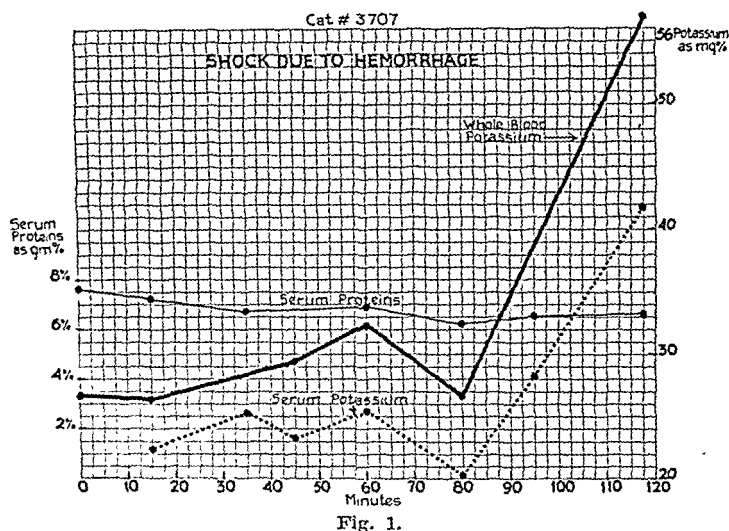


TABLE I (CONT'D)

EFFECT OF REPEATED WITHDRAWAL OF HEART BLOOD ON SPECIFIC GRAVITY OF BLOOD, BLOOD PRESSURE, SERUM, AND WHOLE BLOOD POTASSIUM

Cat 3752. Adult, male  
Dec. 17, 1937

TIME	AMOUNT BLOOD REMOVED	WHOLE BLOOD K MG. % HEART	SERUM K MG. % HEART	SPECIFIC GRAVITY BLOOD HEART	BLOOD PRESSURE SYSTOLIC	REMARKS
P.M. 3:50	(Tied on board and, under local anesthetic, femoral artery exposed for recording blood pressure)					
4:00					120	
4:05	10 c.c.	22.6	19.4	1.0473	136	Blood from heart
4:10					154	
4:17						
4:20	10 c.c.	20.4	17.6	1.0463	110	Blood from heart
4:25					110	
4:30	10 c.c.	20.8	17.7	1.0448	98	Blood from heart; beginning of panting
4:35					85	Blood from heart
4:40	10 c.c.	16.4	15.9	1.0435	88	Passed urine
4:45					58	
4:50	5 c.c.	18.3	18.2	-	62	Blood from heart
4:52						Marked panting with tongue out
5:03					78	
5:10	10 c.c.	17.8	18.3	1.0403	64	Blood from heart
5:15					40	
5:20				1.0380	44	Blood from femoral artery
5:22	10 c.c.	16.6	15.7	1.0395	40	Pallor of tongue and mucous membranes; panting; sluggish response to stimuli; allowed to remain in this state
6:45	10 c.c.	48.1	45.7	1.0149	0	Blood withdrawn just as animal expired



TABLE I (CONT'D)  
EFFECTS OF ARTERIAL BLOOD LOSS

*Cat 3701. Weight 3.94 Kg.*

*Sex: Male*

*Feb. 15, 1937*

TIME	RELATIVE TIME	AMOUNT REMOVED	WHOLE BLOOD K MG. %	SERUM POTAS-SIUM MG. %	SERUM CA MG. %	SPECIFIC GRAVITY WHOLE BLOOD	SERUM SP. GR.	SERUM PROTEIN GM. %
A.M.	Under light ether anesthesia femoral artery exposed for bleeding							
11:20	0	10 c.c.	—	15.4	12.9	1.0518	1.0292	7.62
11:35	15 min.	10 c.c.	21.7	16.0	12.6	1.0518	1.0289	7.52
11:45	25 min.	10 c.c.	23.0	15.3		1.0494	1.0283	7.3
11:55	35 min.	10 c.c.	21.9	14.4	11.9	1.0486	1.0278	7.13
P.M.								
12:07	47 min.	10 c.c.	22.7	15.1	11.4	—	1.0273	6.96
12:20	1 hr.	10 c.c.	21.3	13.9	11.0	1.0451	1.0251	6.2
12:30	1 hr.							
	10 min.	10 c.c.	23.1	17.1	10.8	1.0440	1.0255	6.33
12:40	1 hr.							
	20 min.	4 c.c.*	—	21.5	—	—	1.0266	6.72
<i>Heart's blood</i>								
12:55	1 hr.	10 c.c.	55.6	40.5	12.7	1.0452	1.0280	7.2
	35 min.							
1:00	1 hr.							
	40 min.							
			Portal vein blood.—57.8 mg. %					
			Pericardial fluid.—41.2 mg. %					

\*Blood did not flow well from artery, because of very low pressure.

REPEATED WITHDRAWAL OF HEART BLOOD\*

*Cat 3707. Weight: 2.665 Kg.*

*Sex: Male*

*Anesthesia: none*

*Jan. 21, 1937*

TIME	AMOUNT REMOVED	WHOLE BLOOD K MG. %	SERUM K MG. %	SERUM SPECIFIC GRAVITY	SERUM PROTEIN GM. %	REMARKS
Jan. 20		28.8(c)†				Fasting, healthy, adult cat
7:20						Tied on board for experiment
Jan. 21						
12:20						
12:30	10 c.c.	26.8	—	1.0293	7.6	
12:45	10 c.c.	26.4	22.2	1.0284	7.3	
1:05	16 c.c.	—	25.3	1.0266	6.7	
1:15	14 c.c.	29.4	23.3	1.0268	6.8	Air hunger
1:30	16 c.c.	32.3	25.3	1.0269	6.8	
1:50	10 c.c.	26.7	20.4	1.0254	6.3	Nictitating mem- brane out
2:05	10 c.c.	—	28.1	1.0259	6.5	Extremities cold
2:25						Convulsion
2:26	10 c.c.	57.4	41.7	1.0265	6.6	Very weak; gasp- ing for air
2:30						Dead
Total		96 c.c.				

\*Calculated original blood volume: 160 c.c.

†(c)—Capillary blood.

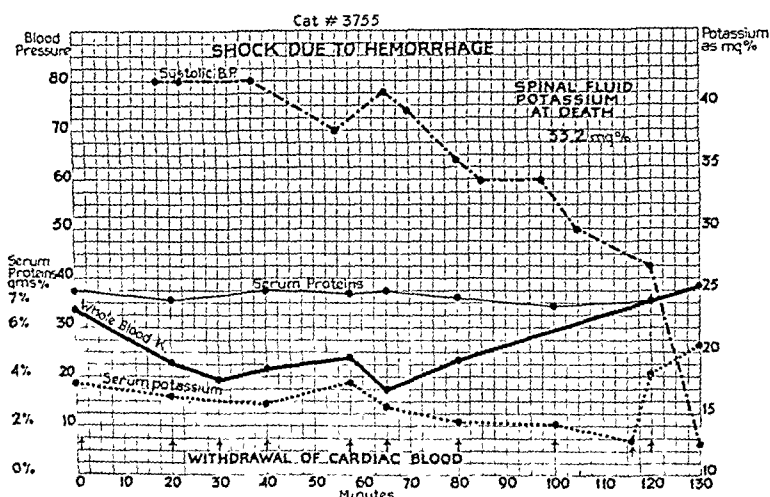


TABLE 1 (CONT'D)

MILD TRAUMA UNDER SODIUM AMYTAL ANESTHESIA  
(70 MG./KG. 1.61 ML. AND 1 ML.)

Cat 3641. Weight: 2,800 Kg.

Sex: female

Oct. 13, 1936

TIME	RELATIVE TIME AFTER TRAUMA	BLOOD K MG. %	SPECIFIC GRAVITY WHOLE BLOOD	REMARKS
A.M. 9:49				
11:05				1.61 ml. Na amytal intraperitoneal
11:30				Cannulation of carotid completed
11:45	0	21.6	1.0440	1 ml. Na amytal intraperitoneal
P.M. 12:00	0	17.3	1.0469	Pound thighs with rubber hammer at 10-min. intervals.
12:11				
12:17	17 min.	14.1	1.0479	
12:25				
12:35				
12:50	50 min.	15.7	1.0481	
1:00	1 hr.*	21.1	(h 1.0486 1.0481	Died suddenly during trouble with clotted canula

\*No marked K changes in 1 hr. with amytal and pounding; cf. Seeley et al.

TABLE I (CONT'D)

EFFECT OF REPEATED WITHDRAWAL OF HEART BLOOD

*Cat 8755. Weight: 3.911 Kg.*

Sex: male

**Anesthesia:** local

Dec. 11, 1937

[illegible]

TABLE I—CONT'D  
 SEVERE TRAUMA UNDER AMYTAL  
*Cat 3640. Weight: 2.522 Kg.*  
*Sex: female*  
*Anesthesia: sodium amytal (70 mg./kg.)*  
*Oct. 18, 1936*

TIME	RELATIVE TIME AFTER TRAUMA- TIZATION	WHOLE BLOOD K AS MG. %	SPECIFIC GRAVITY WHOLE BLOOD	SYSTOLIC BLOOD PRESSURE	TEMPER- ATURE (RECTAL)	PULSE	REMARKS
A.M.							
9:47							1.76 ml. Na amy- tal intraperito- neal
10:30							Cannulation of carotid finished; 10 ml. blood lost 1 ml. Na amytal intraperito- neally
11:25	0	15.2	1.0462	120			
P.M.							
12:30	0	22.1	1.0447				
12:45					96°		Crush and pound left hind leg
1:20	35 min.	24.8	1.0486		95.8°		
1:33					95.0°		
1:35							Pound both legs
1:46							Pound both legs
1:58					96.1°		
2:10	1 hr. 25 min.	22.5	1.0487				
2:25				110			Pound both legs
2:40	1 hr. 55 min.	39.4	1.0485			120	
3:05				110	101.0°		Pound both legs
3:07							Pound both legs
3:25							Anticoagulant 25% $\text{Na}_2\text{S}_2\text{O}_4$ run in
3:28				130			
3:55				85	101.4°		
4:00	3 hr. 15 min.	19.3	1.0487				
4:25				60	101.6°	160	
4:30	3 hr. 45 min.	36.5(h)	1.0496(h)	60	103.0°		
4:33							Dead

TABLE I (CONT'D)

## TRAUMA UNDER AMYTAL\*

Cat 3644. Weight: 3,600 Kg.

Sex: female

Oct. 22, 1936

TIME	RELATIVE TIME AFTER INJECTION OF AMYTAL	WHOLE BLOOD K MG. %	REMARKS
A.M.			
11:00	0	27.5	Healthy, adult, female
11:18	18 min.	24.8	2.5 ml. 10% Na amytal (70 mg. kg.)
11:25			Animal unconscious
11:35			Temperature, 99.6°; heart rate, 200; respira- tions, 24
11:37	37 min.	26.3	Crushed left hind leg by pounding
P.M.			
12:30	1 hr. 30 min.	22.9	
12:40			Right thigh pounded
12:45			Temperature, 97.8°; heart rate, 171; respira- tions, 26
1:00	2 hr.	24.7	
1:30	2 hr. 30 min.	24.3	Temperature, 99.0°; heart rate, 198; respira- tions, 40

\*No change in K under amytal in spite of pounding of legs.

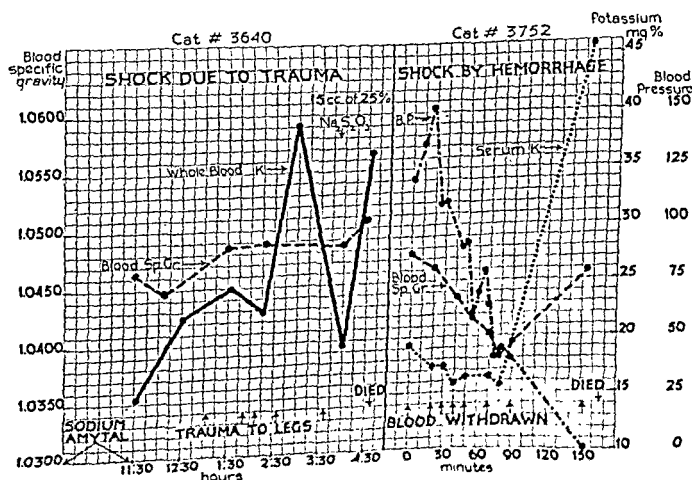


Fig. 3.

TABLE I (CONT'D)

EFFECT OF SEVERE MUSCLE TRAUMA AND MULTIPLE FRACTURES UNDER ETHER—  
CONT'D

TIME	RELATIVE TIME	CAPILLARY BLOOD K AS MG. %	SPECIFIC GRAVITY CAPILLARY BLOOD	WEIGHT % LOSS	REMARKS
5:35	14 hr. 25 min.	33.0	1.0568		Legs massaged; respirations, 112 irregular
6:10	15 hr.	40.5			
6:15	15 hr. 5 min.				Dead

*Autopsy.*—Severe muscle trauma with some extravasation of blood; ruptured muscles very dry  
 Compound fracture of both right and left humerus  
 Compound fracture of right femur  
 Compound fracture of left tibia and fibula  
 Lungs: collapsed; petechial hemorrhages on surface  
 Heart: in diastole  
 Stomach: dilated; contained hair ball but not fluid  
 Small intestine: cyanotic  
 Large intestine: filled with hard feces  
 Liver: red, soft, slightly mottled  
 Spleen: red, leathery in consistency  
 Kidneys: large, soft, pale brown  
 Adrenals: soft, tan color  
 Bladder: partially filled

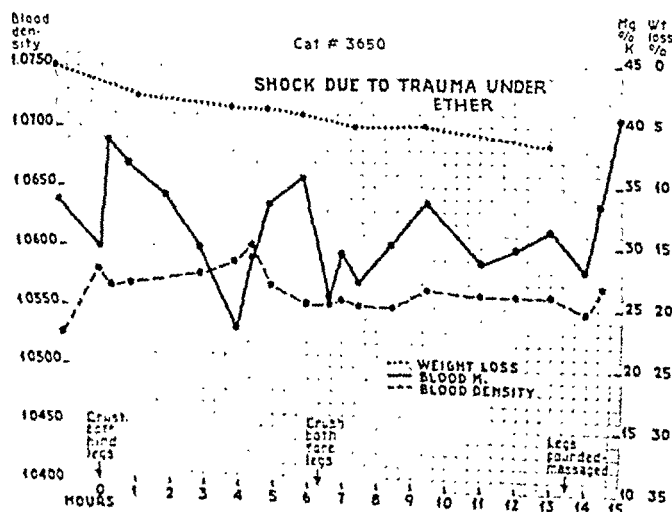


FIG. 4.

TABLE I (CONT'D)

EFFECT OF SEVERE MUSCLE TRAUMA AND MULTIPLE FRACTURES UNDER ETHER

Cat 3650. Weight: 3.686 Kg.

Sex: male, adult

Dec. 7, 1936

TIME	RELATIVE TIME	CAPILLARY BLOOD K AS MG. %	SPECIFIC GRAVITY CAPILLARY BLOOD	WEIGHT % LOSS	REMARKS
P.M.					
2:30		33.8	1.0535		Fasting
3:10	0	Under ether anesthesia, both hind legs crushed			
3:20	10 min.	29.9	1.0579		Respirations, 104
3:40	30 min.	38.2	1.0566		Respirations, 190; panting
4:10	1 hr.	36.6	1.0568	3.600 -2.5%	
5:10	2 hr.	34.2			Restless
6:15	3 hr. 5 min.	29.7	1.0576		
7:10	4 hr.	23.1	1.0587	3.572 -3.2%	Ears cold; blood dark and flows slowly
7:25					Respirations, 38
7:45	4 hr. 35 min.	28.6	1.0601		Blood very dark; respirations, 35
8:25	5 hr. 15 min.	33.5	1.0568	3.560 -3.5%	Ears and extremities cold
9:20	6 hr. 10 min.	35.8	1.0553	3.543 -4.0%	
9:40	6 hr. 30 min.	Under ether anesthesia, right front leg crushed			
9:45	6 hr. 35 min.		1.0553		
10:00	6 hr. 50 min.	25.7			Respirations, 40
10:25	7 hr. 15 min.	29.3	1.0556		Much salivation
10:55	7 hr. 45 min.	27.0	1.0551	3.500 -5.0%	
11:50	8 hr. 40 min.	30.0	1.0550		Blood flow poor; pulse, 200
Dec. 8					
A.M.					
12:50	9 hr. 40 min.	33.6	1.0565	3.500 -5.0%	Blood clots readily
2:10	11 hr.	28.7	1.0560		Condition same
3:10	12 hr.	29.9	1.0560		
4:10	13 hr.	31.3	1.0560	3.450 -6.5%	
4:15	13 hr. 5 min.				Pericardial fluid, 49.8 mg. %
		Heart blood			
4:18	13 hr. 8 min.	31.5			5 c.c. withdrawn
4:40	13 hr. 30 min.	Ether anesthesia, legs traumatized and massaged			
4:55	13 hr. 45 min.	28.0	1.0517		Convulsion

TABLE I (CONT'D)

EFFECT OF MANIPULATION OF INTESTINES WITH ADRENALS TIED OFF

*Cat 3706. Weight: 3.742 Kg.*
*Sex: male*
*Anesthesia: ether*
*Jan. 21, 1937*

TIME	RELATIVE TIME	CAPILLARY BLOOD K AS MG. %	CAPILLARY BLOOD SPECIFIC GRAVITY	REMARKS
Jan. 20				
7:15		25.8		Healthy, adult, nonfasting cat
Jan. 21				
A.M.				
11:00	0	22.1	1.0553	Fasting; tied on board
11:15				Ether anesthesia, operation
11:25				Both adrenal glands tied off
11:30	15 min.	17.6	1.0551	Heart rate, 220; respirations, 28
				Rough manipulation of intestines
11:45	30 min.			Operation finished
11:50	35 min.	21.4	1.0483	Nictitating membranes out
P.M.				
12:15	1 hr.	28.3		Recovered from anesthesia. Marked asthenia; some oozing of blood from wound
12:45	1 hr. 30 min.	19.5	1.0498	Defecated
1:35	2 hr. 20 min.	22.1		Struggled
2:10	2 hr. 55 min.	38.5	1.0528	Extremities cold; in shock
		Heart blood	Heart blood specific gravity	
4:00	4 hr. 45 min.	22.4	1.0503	Extremities cold
5:00	5 hr. 45 min.	25.8	1.0543	Labored breathing, rate 98; extremities cold.
5:55				Very restless
6:05	6 hr. 50 min.	30.6	1.0544	Very weak; died shortly after taking blood
<i>Autopsy.</i> —Lungs: collapsed, pink; no fluid in pleural cavity				
Heart: some bloody fluid found in pericardial cavity				
Peritoneal cavity: much bloody fluid; serosa showed trauma, with extravasation of blood				
Intestines: contracted with extensive subserosal hemorrhage; thin fibrinous adhesions present; the ligatured adrenals pale				
Kidneys: soft, swollen, brown in color; bladder filled				



TABLE I (CONT'D)  
EFFECTS OF INTESTINAL MANIPULATION

*Cat 3702. Weight: 3.657 Kg.*

*Sex: male*

*Anesthesia: ether*

*Jan. 11, 1937*

TIME	RELATIVE TIME AFTER MANIPULA- TION	CAPILLARY WHOLE BLOOD K AS MG. %	SPECIFIC GRAVITY CAPILLARY BLOOD	REMARKS
Jan. 9				
5:45	0	26.0	—	Fresh, healthy adult
Jan. 11				
P.M.				
12:40	0	25.0	1.0512	Nonfasting; weight, 3856 gm.
12:45	Operation under ether; viscera manipulated in a towel for 25 min.;			
1:15	abdomen closed; weight, 3,800 gm.			
1:20	5 min.	24.9	1.0500	Respirations, 180
1:35				Respirations, 260; urinated and vomited much food
2:20	1 hr. 5 min.	19.6	1.0483	Respirations, 182; vomited thin brownish fluid
				Weight, 3,457 gm.
2:20				
3:20	2 hr. 5 min.	22.9	1.0512	Weight, 3,429 gm.; mucous membranes dry
3:40				Respirations 60, irregular; weight: 3,417 gm.
4:20	3 hr. 5 min.	34.3	1.0529	Respirations 100; blood obtained with some difficulty
5:00	3 hr. 45 min.	Heart blood 24.2	Heart blood 1.0508	
		Heart serum 26.0	1.0535	
6:30	5 hr. 15 min.	Heart blood 41.0	1.0518	Dead
7:45	6 hr. 30 min.	Peritoneal fluid 57.1		

*Autopsy.*—Peritoneal cavity filled with bloody fluid. Intestines contracted. Much subserosal ecchymoses where gut was handled. Liver and spleen leathery in consistency. Gall bladder filled. Pancreas pale. Kidneys tense and swollen. Adrenal cortex gray and shrunken; hemorrhage between cortex and medulla. Heart in diastole. Lungs pink and collapsed with few petechial hemorrhages on surface.

TABLE II  
WHOLE BLOOD K IN SECONDARY SHOCK IN CATS.

CAT NO.	INITIAL K MG. %	PROCEDURE USED TO PRODUCE SHOCK	TIME OF SURVIVAL	K VALUE IN SHOCK MG. %	TOTAL NUMBER OF SAMPLES TAKEN
3655	27.7	50 cm. strangulated loop	9 hr.	36.4	9
3630	27.5	Jejunal loop	14 hr.	39.3	9
3631	20.2	20 cm. strangulated loop	30 hr.	66.6	15
3632	17.3	Anemic jejunum loop	45 hr.	29.6	5
3713	22.7	Duodenostomy	3 days	44.2	11
3636	30.0	Esophageal obstruction	3½ days	52.0	11
3639	21.8	Duodenal obstruction	3½ days	39.7	11
3718	35.6	Duodenostomy	4 days	61.5	18
3712	29.1	Jejunostomy	4 days	84.0	9
3717	37.1	Jejunostomy	4 days	86.6	9
3721	25.5	Gastrostomy	5 days	37.5	11
3724	22.6	Gastrostomy	5 days	40.9	16
3709	19.8	Ileostomy	5 days	84.8	10
3649	24.3	Pancreatitis	5 days	52.3	10
3638	31.7	Duodenal obstruction	7½ days	42.6	16
3710	21.1	Ileostomy	10 days	48.0	21

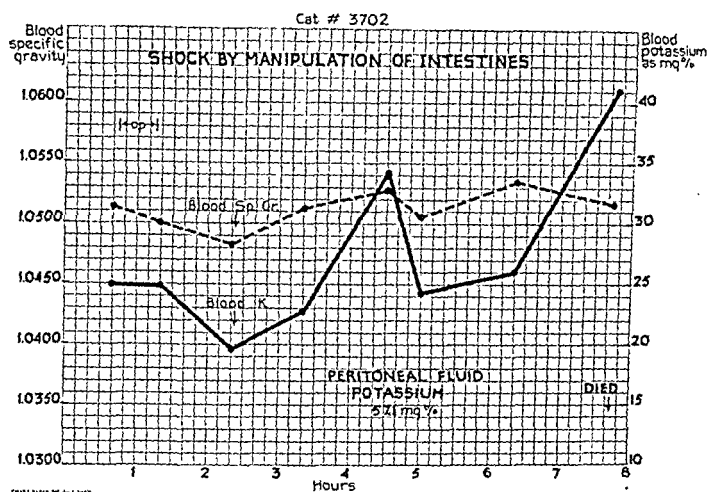
In attempting to correlate the divergent theories concerning the causes of death in adrenal insufficiency (Zwemer and Truszkowski, 1937), intestinal obstruction (Seudder, Zwemer, and Truszkowski, 1937), and intestinal fistulas (Seudder and Zwemer, 1937) consideration of potassium as the unknown toxin seemed to make the various explanations more compatible. Since in a condition of shock our present data show a rise in blood potassium to high levels, it seems reasonable to believe that inadequate potassium regulation is also a factor which must be considered in any explanation of shock.

#### SUMMARY

The remarkably constant regulation of potassium by the body is altered during the condition of shock. Fluctuations suggest alternate success and failure of regulation, and a sudden increase precedes death. Peripheral blood samples are not always indicative of the changes taking place internally, especially in the fluids of closed cavities, such as pericardial and cerebrospinal fluids (Table III).

TABLE III  
POTASSIUM CONTENT OF SOME BODY FLUIDS AT TIME OF DEATH FROM SHOCK

Cerebrospinal fluid	32.9 mg. % K
Lymph	30.3 mg. % K
Pericardial fluid	49.8 mg. % K
Peritoneal fluid	57.1 mg. % K
Traumatized tissue fluid	77.9 mg. % K



beds, to capillary leakage and filling of tissue spaces, or finally to a loss of extracellular body fluids by hydration of cells. Maintenance of a constant body weight would favor the explanations of internal redistribution; whereas, a weight decrease would strengthen the view of anhydremia by actual fluid loss from the body.

Others believe that the presence of some toxin is necessary to explain all of the phenomena. This toxin was first thought to be histamine, but the term "H" substance is now generally used for this histamine-like constituent of tissues which is released by injury. It is probable that potassium is an important "H" substance always available.

The relation of adrenal cortex function to shock is attested by an extensive literature. Treatments of various types of shock, such as traumatic (Swingle and Parkins, 1935), anaphylactic (Wolfram and Zwemer, 1935; Dragstedt and others, 1937), histamine (Wyman and Tum Suden, 1937), and the toxin of intestinal obstruction (Heuer and Andrus, 1934; Wohl and others, 1937) are represented. The evidence that potassium regulation is a function of the adrenal cortex (Zwemer and Sullivan, 1934; Zwemer and Truszkowski, 1936, 1937; Truszkowski and Zwemer, 1938) is receiving increasing support (Allers, 1936; Harrop, 1936; Nilson, 1937; Thorn, 1937). Since a marked increase in extracellular potassium is injurious to cells and injured cells lose potassium, a vicious cycle ending in death may be initiated if the plasma K is allowed to rise. Therefore, rational therapy for shock should include measures which enable the body to restore and maintain a normal potassium level in body fluids. These are sodium salt therapy, adequate but not excessive fluid administration (Seudder, Zwemer, and Whipple, 1938), and cortin therapy.

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Detailed data from twelve cats (Table I), and supplementary information from sixteen other animals (Table II) are presented.

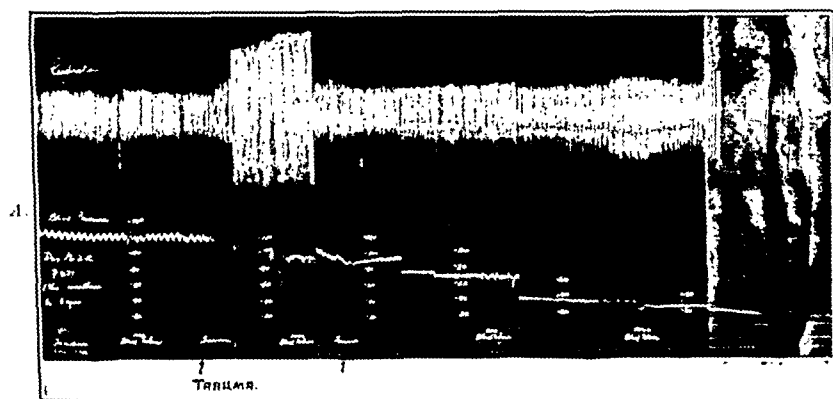
We take this opportunity to thank Dr. Richard Truszkowski for his assistance in the amytal experiments.

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ing manometers mounted on a kymograph. Continuous records of respiration, pulse rate and blood pressure were made throughout the experiments. Portions of these records are shown in Figs. 1A and 2A.

Because sodium citrate was used in the system connecting the carotid artery and manometer, it was possible for minute quantities of sodium



Dog 28 Traumatic Shock

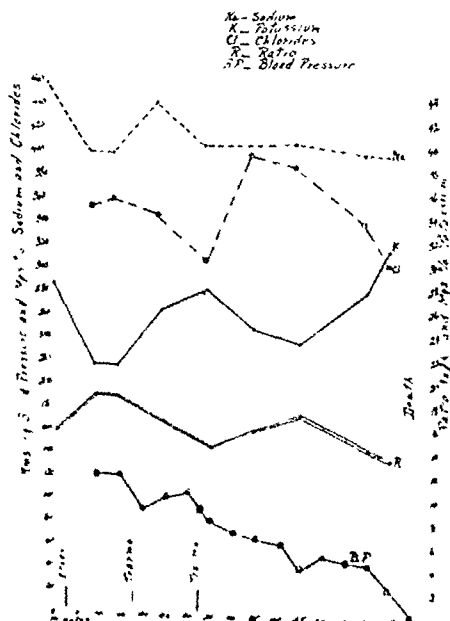


Fig. 1—Dog 28. A, Sections from a continuous kymographic record showing changes of pulse, blood pressure, and respiration with progressive development of traumatic shock. B, Graphic record of changes of blood pressure recorded in A and of serum sodium, potassium, and chlorides during the development of traumatic shock. Note fall of sodium and potassium with induction of ether anesthesia, a sharp rise to nearly normal levels after trauma and, after a second recession, a rise of potassium to a level slightly above normal as shock became profound.

# STUDIES OF SODIUM, POTASSIUM, AND CHLORIDES OF BLOOD SERUM IN EXPERIMENTAL TRAUMATIC SHOCK, SHOCK OF INDUCED HYPERPYREXIA, HIGH INTESTINAL OBSTRUCTION, AND DUODENAL FISTULAS

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IN VIEW of the profound disturbances of tissue metabolism, blood volume, and water balance associated with traumatic shock, hyperthermic shock, and high intestinal obstruction, chemical alterations of the blood would seem inevitable. There has accumulated much evidence to show that this is true.

This investigation had for its purpose the determination of the extent to which certain of these changes, namely the alterations in the relative proportions of serum sodium and potassium, play in the production of symptoms and in the cause of death. It will be observed from an analysis of the results that there exists no constant relationship, also that the quantitative changes in both sodium and potassium appear to be incidental to the changes in blood volume and concentration rather than the cause of the prostration and death.

## EXPERIMENTS

Sixteen dogs were used for nineteen experiments. Chemical analyses were made upon blood serum from blood aspirated from the heart. In one animal, for purposes of comparison, determinations were made upon both whole blood and serum from samples of blood taken simultaneously. Contrary to certain reports, we found a wide variation in the content of sodium and potassium in serum as compared to whole blood. Blood chlorides were determined by the method described by Saifer and Kornblum and the sodium and potassium by a modification of the methods of Kramer and Tisdall and Saht described by Morgulis and Perley. With only a few exceptions, each analysis was run in duplicate.

## TRAUMATIC SHOCK

After taking blood for normal control determinations, 3 animals were anesthetized with ether and traumatic shock was induced by confusing both lower extremities. In 2 animals, Dogs 1R and 2R, the trachea and carotid artery were cannulated and connected to record-

Detailed analyses of the results of the experiments are shown in Figs. 1A and B, 2A and B. They consistently showed the following changes: (1) A sharp fall of both sodium and potassium with the induction of ether anesthesia. (2) A slight rise but continued subnormal level of both sodium and potassium with the progressive fall in blood pressure until the degree of shock became profound and terminal. There was then a sharp rise of potassium in all animals. In one, Dog 1R, it mounted to an extremely high level; in another, Dog 2R, to a level slightly above the preoperative level; and in the third, Dog 4L, it never reached the preoperative level. In Dog 1R adrenalin was given intracardially 1½ minutes before the first blood sample, which showed a very high level of potassium, was taken. In this case we believe that the adrenalin was probably at least partially responsible for this response because simultaneously there was a precipitous rise of blood pressure. (3) No significant changes in blood chlorides. (4) The sodium-potassium ratio rose with induction of anesthesia and progressively fell as the blood pressure dropped.

#### INDUCED HYPERPYREXIA

In 4 dogs fever was induced and made to progress to a lethal degree in a heat chamber of Kettering design. As in the preceding experiment, continuous kymographic records were made of respirations, pulse, and blood pressure in 2 animals but omitted in 2 dogs to avoid the possible influence of the sodium in sodium citrate used in the manometric system. The anesthesia consisted of amytal administered orally and supplemented by ether induction.

Composite data of the experimental results are shown in Fig. 3A and B and in Tables I and II. They may be summarized as follows: (1) Induced fever became lethal at 112° F. (2) Blood pressure began to fall as the temperatures reached 104° and fell rapidly to shock levels as temperatures mounted above 108°. (3) Potassium fell with the induction of anesthesia and then rose to levels of 30 to 50 per cent above the normal control levels with the induction of fever.

TABLE I  
Dog 500—HYPERTHERMIC SHOCK

	RECTAL TEMPERATURE	SODIUM MG. %	CHLORIDES MG. %	POTASSIUM MG. %	CALCIUM MG. %
1. Normal control	100.8	270	359	15.2	11.2
2. After induction of anesthesia		274	347	14.2	11.46
3. Hyperthermia, 30 min.	108.2	245	333	12.8	10.70
4. Hyperthermia, 55 min.	110.2	267	374	20.2	9.83
Experimental error		+ or -5%	+ or -2%	+ or -3%	+ or -1%



to enter the blood stream. For this reason the blood studies in the third animal, Dog 4L, were made without recording blood pressure. Since in this animal the analyses did not differ significantly from those in which blood pressure records were made, it would appear that if sodium entered the blood stream it did so in too small quantities to influence the levels of sodium and potassium of the serum.

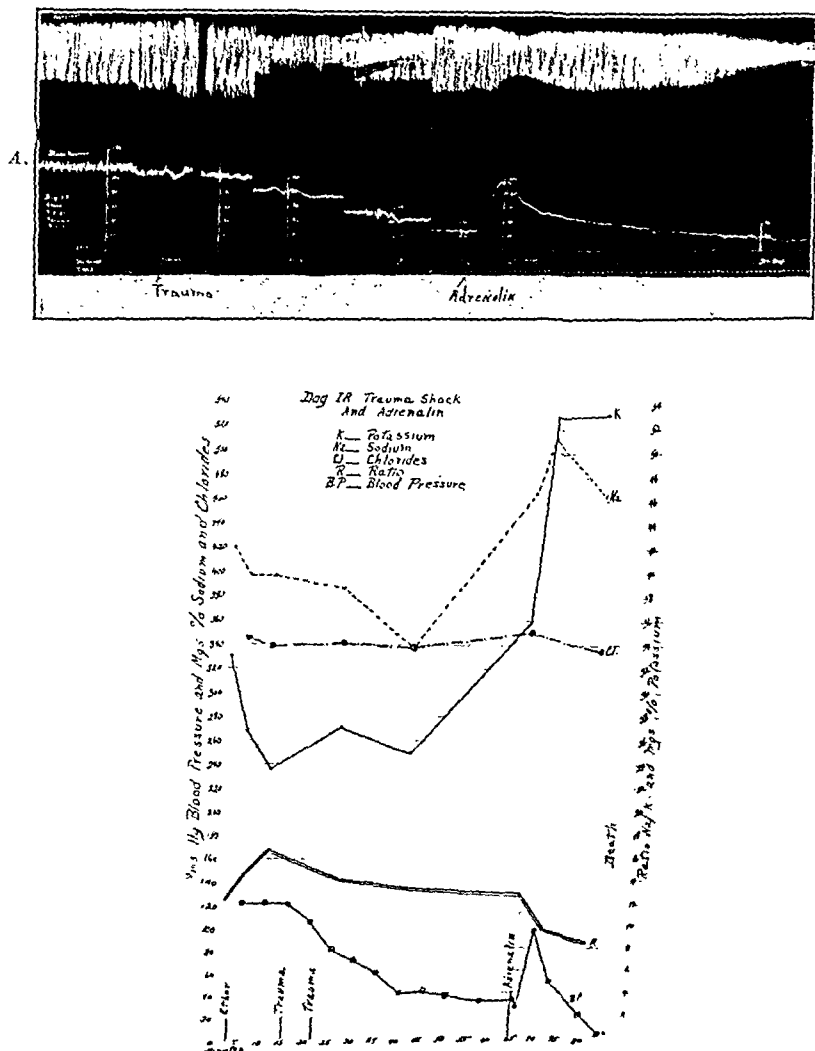


Fig. 2.—Dog 1R. A, Sections from a continuous kymographic record of induced traumatic shock. When the blood pressure had fallen to 30 mm. Hg. 7 mins. of adrenalin was given intracardially. Immediately the pressure rose to 95 mm. and then fell progressively to zero with death. B, Plotted with the blood pressure curve taken from the kymographic record illustrated in A are the concomitant fluctuation of serum sodium, potassium, and chlorides. Note the initial fall of sodium and potassium with induction of anesthesia, the gradual return to preoperative levels with development of shock, and then the precipitous rise to very high levels with the elevation of blood pressure which followed injection of adrenalin.

Detailed analyses of the results of the experiments are shown in Figs. 1A and B, 2A and B. They consistently showed the following changes: (1) A sharp fall of both sodium and potassium with the induction of ether anesthesia. (2) A slight rise but continued subnormal level of both sodium and potassium with the progressive fall in blood pressure until the degree of shock became profound and terminal. There was then a sharp rise of potassium in all animals. In one, Dog 1R, it mounted to an extremely high level; in another, Dog 2R, to a level slightly above the preoperative level; and in the third, Dog 4L, it never reached the preoperative level. In Dog 1R adrenalin was given intracardially 1½ minutes before the first blood sample, which showed a very high level of potassium, was taken. In this case we believe that the adrenalin was probably at least partially responsible for this response because simultaneously there was a precipitous rise of blood pressure. (3) No significant changes in blood chlorides. (4) The sodium-potassium ratio rose with induction of anesthesia and progressively fell as the blood pressure dropped.

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2. After induction of anesthesia		274	347	14.2	11.46
3. Hyperthermia, 30 min.	108.2	245	353	12.8	10.70
4. Hyperthermia, 55 min.	110.2	267	374	20.2	9.83
Experimental error		+ or -5%	+ or -2%	+ or -3%	+ or -1%

TABLE II  
DOG 502—HYPERTHERMIC SHOCK

	RECTAL TEMPERATURE	SODIUM MG. %	CHLORIDES MG. %	POTASSIUM MG. %	CALCIUM MG. %
1. Normal control	101.4	286	368	12.4	9.92
2. After induction of anesthesia		274	354	12.5	11.1
3. Hyperthermia, 40 min.	106.0	254	360	6.5	10.37
4. Hyperthermia, 55 min.	106.8	262	371	8.3	10.65
5. Hyperthermia, 60 min.	107.5	255	373	10.5	10.46
6. Hyperthermia, 65 min.	108.0	258	375	12.9	10.24
7. Hyperthermia, 90 min.	110.0	282	373	12.9	10.15
8. Hyperthermia, 115 min.	111.8	282	380	14.9	10.18
Experiment error		+ or -4%	+ or -2%	+ or -5%	+ or -1%

The rise in potassium roughly paralleled the rise in fever in 3 animals, but in 1 it reached a maximum at a temperature of 106° and, although it then fell, it remained above the control level until the animal was in extremis. (4) Sodium and chlorides remained relatively unchanged in 3 dogs. In 1 the sodium fell consistently, falling to nearly one-half of its control level. (5) The sodium-potassium ratio showed a slight rise with induction of anesthesia and a fall with development of fever and shock.

Determinations of serum calcium were made in 2 dogs. In both a slight rise with induction of anesthesia was followed by a slight fall to the normal initial level or slightly below it.

#### INFLUENCE OF ETHER ANESTHESIA AND ADRENALIN

Determinations of these influences were undertaken because the serum potassium had shown a sharp drop constantly and consistently with induction of ether anesthesia in the experiments described above and had mounted to an excessively high level immediately after the administration of adrenalin in the one dog which received it while in profound shock.

The results are shown in the graphs, Fig. 4A-C. With both ether and adrenalin, potassium fell sharply but transiently and returned promptly to the normal control levels. At no time did the potassium rise above the normal control levels. Sodium and chlorides showed no significant change. The ratios of sodium and potassium varied inversely with the fluctuations of potassium.

#### HIGH INTESTINAL OBSTRUCTION

At varying levels and by various means, the duodenum was completely obstructed in 5 animals and the duodenum and proximal jejunum in 2 animals.

1. *Obstruction by Division.*—In 2 dogs obstruction was produced by severing the bowel and turning in the ends with two rows of sutures. In 1 dog the obstruction was made just below the pylorus; in the

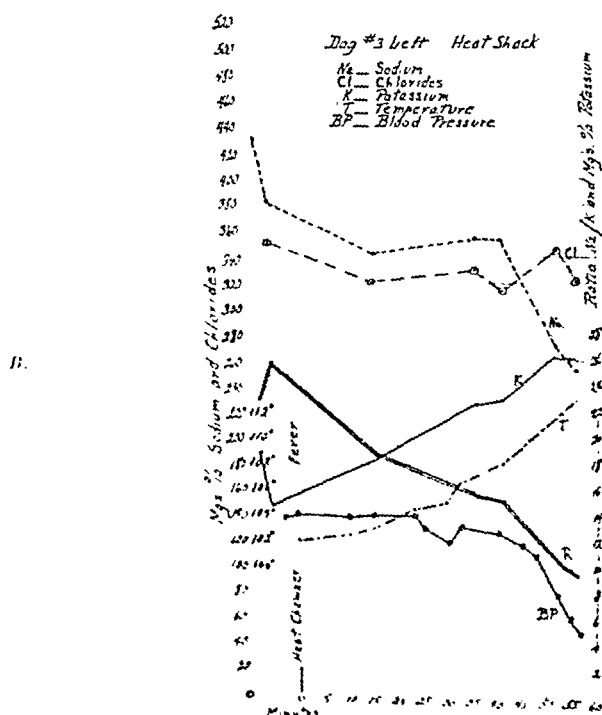
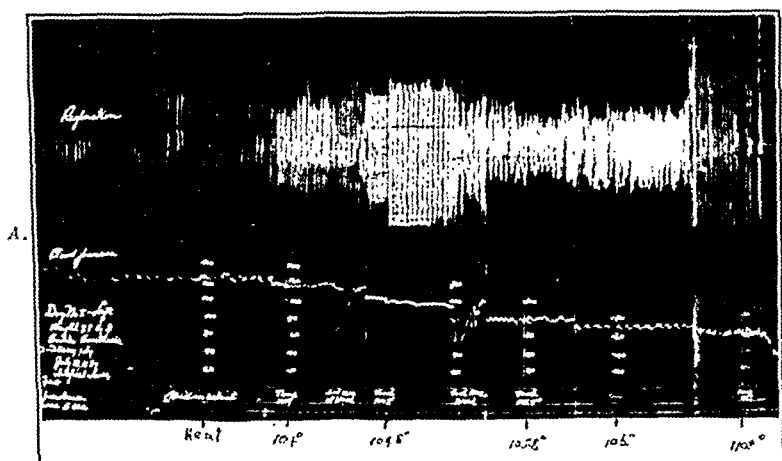


FIG. 5. Dog 31. A, Sections from a continuous kymographic record showing the progressive increase of both pulse and respiratory rates and progressive fall of blood pressure associated with the increasing hyperpyrexia. Respirations became profoundly increased in respect to both rate and amplitude. B, A composite graph of development of hyperpyrexia to its fatal termination. Note the parallel rises of temperature and potassium.

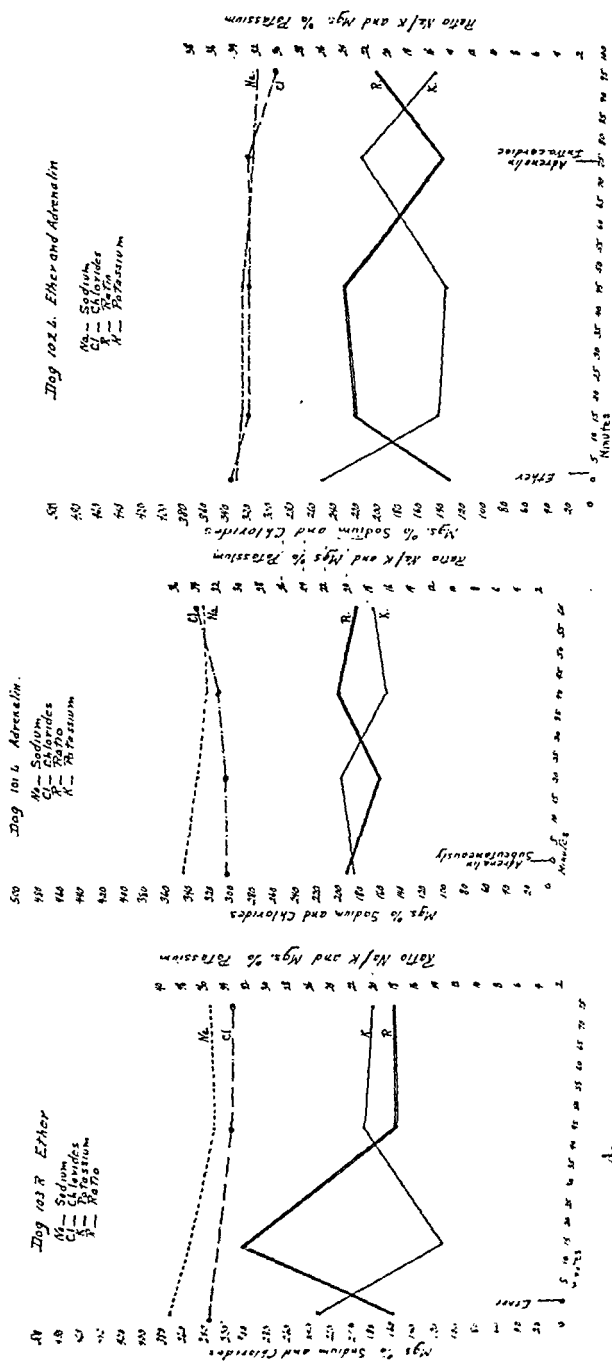


Fig. 1—A. Changes in serum sodium, potassium, and chloride associated with ether inhalation anesthesia. Note abrupt initial drops followed by a rise but failure to regain the normal preoperative levels. B. Changes in serum sodium, potassium, and chloride following subcutaneous administration of 1 c.c. of adrenalin, 1:1,000. Note slight fall in potassium. C. The response to both ether 0.5 c.c. of adrenalin, 1:1,000. After the serum potassium had returned almost to its original normal preanesthetic level, intracardiac adrenalin was given intracardially. Note that this was followed immediately by a second drop in the level of potassium.

other, a few centimeters below the ampulla of Vater. Thus, in the dog with pyloric obstruction only gastric secretions were excluded from the intestinal tract. Bile and pancreatic and intestinal secretions could move down the tract unobstructed, but in the latter animal all of these secretions likewise were excluded. However, the dog with

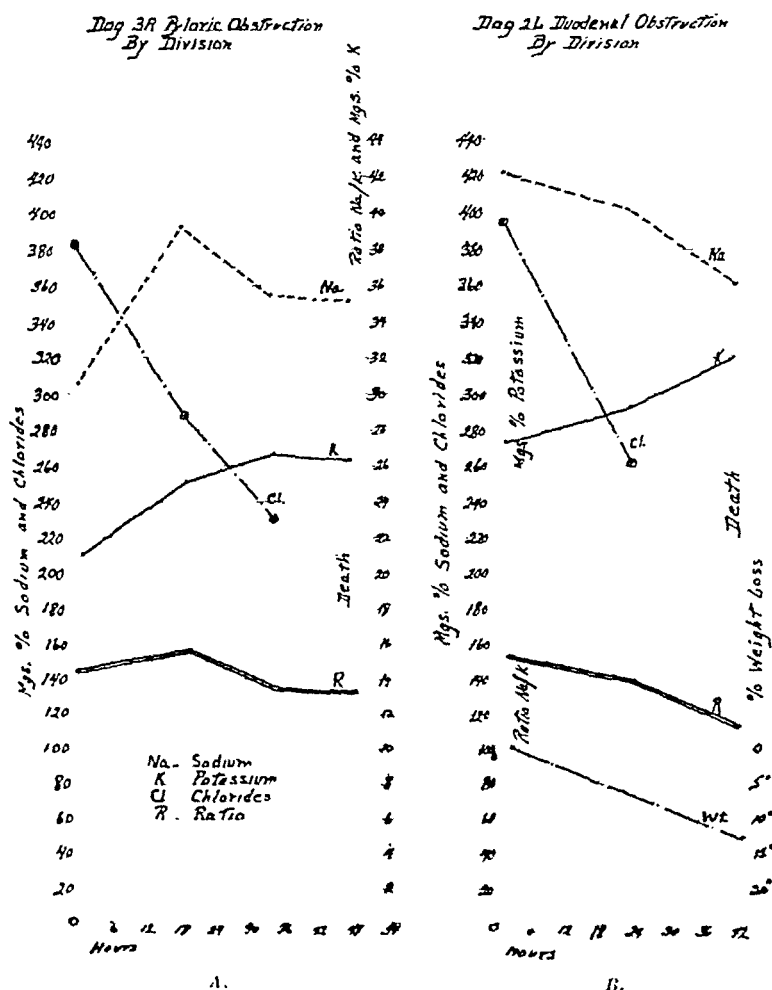


Fig. 5.—A, Pyloric obstruction by division. Note the large decrease in chlorides and a small but sustained increase of potassium. B, Duodenal obstruction by division; a marked decrease in chlorides and a small progressive increase in potassium.

obstruction above the ampulla lived 52 hours, 10 hours longer than the one obstructed below it.

As shown in the Protocols 1 and 2 and in Fig. 5A and B, there was consistently a precipitous fall in chlorides, a rise of potassium to 18 and 26 per cent above preoperative levels, and a slight fall in the sodium-potassium ratio. In the animal with pyloric obstruction there



tion was released and spontaneous anastomosis occurred. The latter animals, after becoming almost moribund, completely recovered.

Consistently in all of these animals there was a large and rapid fall of chlorides and a lesser fall of sodium. Potassium increased from 18 to 30 mg. per cent in the dog which developed peritonitis but in the other 2 it not only promptly fell below the preoperative level but also remained below that level. The sodium-potassium ratios in all 3 animals varied inversely with the levels of potassium and all lost weight, 1 as much as 23 per cent. See Figs. 6A and B and 7 and Protocols 3, 4, and 5.

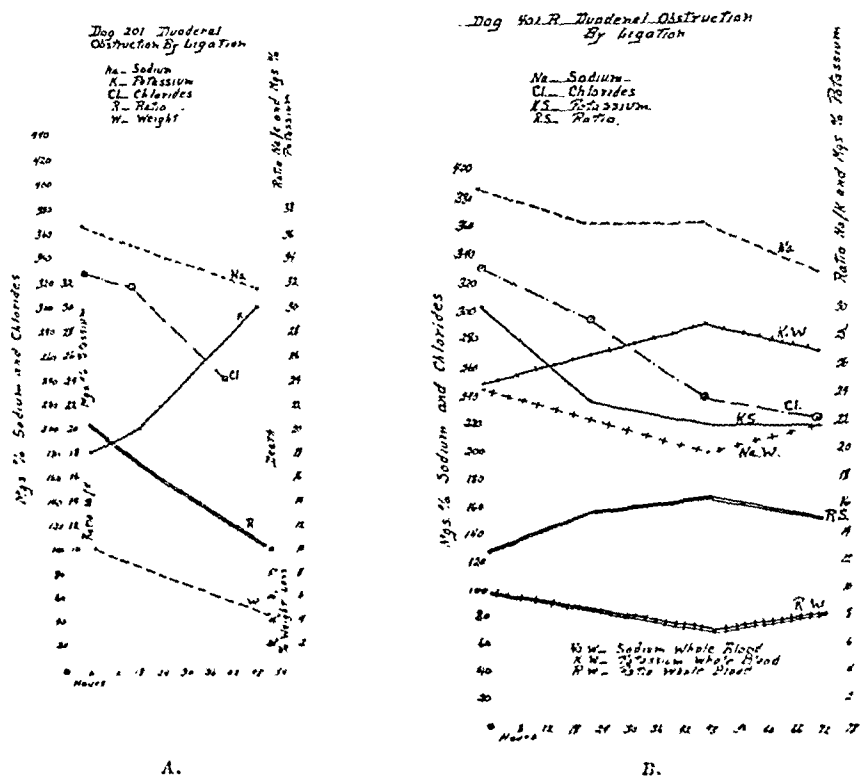


Fig. 6.—A, Duodenal obstruction by ligation. A large progressive decrease in chlorides and a large terminal increase in potassium. In addition to obstruction, autopsy revealed peritonitis. B, Duodenal obstruction with recovery. In general this experiment parallels that illustrated in Fig. 7. Determinations of sodium and potassium were made upon both serum and whole blood. The values are in no way comparable.

The records of 2 of these dogs deserve individual comment.

Dog 101R, 96 hours after simple ligation of the duodenum 4 cm. below the ampulla of Vater, became so weak that it was unable to stand. The mouth was dry and the eyes were covered with a thick mucoid discharge. Muscle groups twitched irregularly throughout the body and there had been a loss of 17 per cent of body weight. Chlorides had fallen from 370 to 196 mg. per cent. Potassium, after



was a rise in sodium, while in the one with obstruction below the ampulla of Vater the sodium fell progressively. The latter animal lost 13 per cent of its body weight.

# PROTOCOL 1

## PYLORIC OBSTRUCTION BY DIVISION

Dog 3R, male; weight, 12.3 kilo. On July 22, 1937, the duodenum was divided immediately distal to the pyloric sphincter and the ends were closed by inversion.

HOURS POSTOPERATIVELY	REMARKS	RECTAL TEMPERATURE	SERUM CHLORIDES	SERUM SODIUM	SERUM POTASSIUM
9	Preoperative	102.0	382	307	21
	Considerable vomiting; dry and slightly apathetic	102.8	288	393	25
26	Weak, unsteady gait; apathetic, dry, gaunt	104.0			
42	Stands unwillingly; eyes contain mucus; muscles twitch	103.0	230	355	26.6
50	Refuses to stand; muscles twitch	101.0		350	26.4
60	Death—Autopsy: peritoneal cavity clean, suture lines tight, stomach contracted, duodenum distended, heart normal, terminal bronchopneumonia both lungs				

2. *Obstruction by Simple Ligation.*—In 3 dogs the duodenum was obstructed immediately below the ampulla of Vater by simple ligation with broad strands of cotton tape. There was no interference with circulation. In all dogs the tape cut through the bowel, resulting in leakage and peritonitis in 1 dog, while in the other 2 the obstruc-

# PROTOCOL 2

## DUODENAL OBSTRUCTION BY DIVISION

Dog 2L, male; weight, 14.47 kilo. On July 22, 1937, the duodenum was divided 5 cm. below the ampulla of Vater and the ends were turned in.

HOURS POSTOPERATIVELY	REMARKS	RECTAL TEMPERATURE	SERUM CHLORIDES	SERUM SODIUM	SERUM POTASSIUM
18	Preoperative	101.8	395	422	27.4
	Vomiting several times; apathy; dehydrated	102.2			
25	Some, but less vomiting; weak, but stands and wags tail slowly	104.0	261	403	29.2
42	Very weak, listless and unable to stand; eyes coated with mucus; irregular twitching of all the muscles	100.0		361	32.0
47	Dead—Autopsy: abdomen dry and clean, suture lines tight, stomach and duodenum collapsed, below obstruction bowel slightly dilated; lungs clear, heart normal				

## PROTOCOL 4

## DUODENAL OBSTRUCTION BY SIMPLE LIGATION

Dog 101R, female; weight, 7.03 kilo. On July 27, 1937, the duodenum was ligated with a broad piece of tape, 4 cm. distal to the ampulla of Vater.

HOURS POSTOPER- ATIVELY	REMARKS	RECTAL TEMPERATURE	SERUM CHLORIDES	SERUM SODIUM	SERUM POTASSIUM
	Preoperative	101.0		346	30.6
7	Vomited several times; slightly apathetic		336	366	29.0
19	Continued vomiting, dry but looks fairly well	102.2	312	362	29.2
22	Dry, weak; has taken no food and little water			371	27.6
26	No change	101.6		366	25.2
42	Vomiting less; much weaker; mucopurulent scum over the eyes	100.1	252	362	24.0
55	Weak, tremulous, very gaunt	100.0	221	332	21.4
74	Sways when standing, staggers and falls	100.4	223	312	26.6
90	Unable to stand, cold, uninterested in surroundings; twitching	100.0	209	317	26.6
105	Nearly moribund; 21% weight loss	100.0	214	321	21.6
139	Spontaneous anastomosis and release of obstruction; much improved; stands, wags tail, drinks water	100.6	209	324	19.0
176	Condition unchanged	100.4	196	293	20.4
188	Relapse, nearly moribund	100.2	196	287	14.6
234	Much improved, appears well but weak, flanks filled out; taking food	101.4	206	331	17.2
288	Continued improvement; appears quite well	102.2	227	348	18.0
360	Jumps about, appears well		309	379	23.2
405			327	375	23.6
502	Regained preoperative weight		332	380	24.7
574	Continued normal appearance	102.2	337	325	27.4

Exploratory operation showed that ligature around bowel had cut through and a spontaneous anastomosis had developed. Apparently this took place simultaneously with recovery from moribund state. As the dog began to take water, the chlorides and sodium dropped slightly, possibly from blood dilution, and then increased rapidly.

From these findings, it would appear that the relative content of potassium in serum and in whole blood does not remain constant and that determinations made upon whole blood do not indicate the changes which take place in serum potassium.

## PROTOCOL 3

## DUODENAL OBSTRUCTION BY SIMPLE LIGATION

Dog 201L, female; weight, 4.74 kilo. On Aug. 3, 1937, the duodenum was ligated 2 cm. distal to the ampulla of Vater with a piece of tape so placed that it did not disturb circulation.

HOURS POSTOPERATIVELY	REMARKS	RECTAL TEMPERATURE	SERUM CHLORIDES	SERUM SODIUM	SERUM POTASSIUM
	Preoperative	101.2	366	345	18.6
7	Vomiting; slightly apathetic	100.4	324	366	18.0
19	Some vomiting; dry; looks quite well	103.2	319	351	20.0
41	Weak, but stands and wags tail; dry	101.8	242		
51	Very weak, refuses to stand; scum over eyes; muscles twitch	102.6		314	30.0
52	Dead—Autopsy: purulent exudate throughout peritoneal cavity but peritonium only slightly injected; ligature cut through bowel wall resulting in leakage; stomach and bowel collapsed; both lungs contained hemorrhagic areas				

an initial drop from 30.5 to 21.4 mg. per cent during the first 55 hours, had regained much of the loss but reached a maximum level of only 29 mg. per cent.

At this time the animal's death seemed imminent, but 24 hours later there was unmistakable evidence of improvement, which lasted about 48 hours. Then there developed a return of symptoms and again death seemed imminent. But at this time, 192 hours, 8 days following operation, something happened and from this time on the animal's condition constantly and rapidly improved. Subsequent exploratory operation showed that continuity of the duodenal lumen had been re-established by spontaneous anastomosis. With the beginning of improvement on the eighth day, the animal began to take water and there followed a sharp rise of sodium and a progressive but slower rise in chlorides. There was no change in the level of the potassium until the animal began to take food 96 hours later or on the twelfth day. It then progressively mounted.

Interestingly, there was no appreciable gain in weight during the first 7 days after the beginning of improvement and of ingestion of water. Before there was a gain in weight the serum sodium and chlorides had returned to nearly normal levels.

In Dog 401R analyses of sodium and potassium were made upon both serum and whole blood from samples drawn simultaneously. The sodium of both serum and whole blood decreased and, when the values were plotted, formed similar curves. The curves of potassium, however, were completely reversed. Potassium of the serum showed a progressive decrease and that of whole blood a progressive increase.

Dog 401R, female; weight, 7.3 kilo.  
HOURS POST-OPERATIVE

DUODENAL OBSTRUCTION BY SIMPLE LIGATION  
PROTOCOL 5

	REMARKS	RECTAL TEMPERATURE	CHLORIDES		SODIUM		POTASSIUM	
			SERUM	WHOLE BLOOD	SERUM	WHOLE BLOOD	SERUM	WHOLE BLOOD
24	Preoperative Vomited several times; weak and dry standing; listless; wobbles when Scum over eyes; Generalized twitching; Very weak; Generalized twitching; No definite change; possibly stronger	101.2	331		386	245	30.2	
48		102.6	293		360	198	23.4	
76		101.9	238		326		21.8	28.9
90	From this time on the animal improved and rapidly regained normal health. At a subsequent post-mortem examination, it was found that a spontaneous anastomosis had been established around the point of obstruction	101.5	221		365	219	21.8	
		100.8	244				20.8	26.5

## PROTOCOL 5

## DUODENAL OBSTRUCTION BY SIMPLE LIGATION

Dog 401R, female; weight, 7.3 kilo. Aug. 24, 1937, the duodenum was ligated 5 cm. distal to the ampulla of Vater with tape.

HOURS POST- OPERATIVELY	REMARKS	RECTAL TEMPERATURE	CHLORIDES		SODIUM		POTASSIUM	
			SERUM	WHOLE BLOOD	SERUM	WHOLE BLOOD	SERUM	WHOLE BLOOD
24	Preoperative Vomited several times; weak and dry Less vomiting; listless; wobbles when standing Seum over eyes; generalized twitching; very weak No definite change; possibly stronger	101.2	331		386	245	30.2	24.8
48		102.6	293		361		23.4	
76		101.9	238		360	198	21.8	28.9
90		101.5	221		326		21.8	
		100.8	244		365	219	20.8	26.5

From this time on the animal improved and rapidly regained normal health. At a subsequent post-mortem examination, it was found that a spontaneous anastomosis had been established around the point of obstruction

3. *Obstruction With Strangulation.*—In 2 dogs the duodenum below the ampulla of Vater and including a small upper segment of jejunum were strangulated by encircling the loop with a piece of tape which was tied with tension sufficient to cause obstruction of the bowel and of venous return but not of the arterial blood supply. The loops were 20 cm. and 12 cm. in length. The dog with the longer loop died in 18 hours, while the one with the short loop survived 27 hours. Each dog lost approximately 10 per cent of its body weight and showed no significant alteration of blood chemistry. The chlorides dropped only slightly and the sodium in each instance, after a transient, abrupt elevation, returned to the normal preoperative levels. Potassium in the dog with the long loop remained unchanged; in the other one it

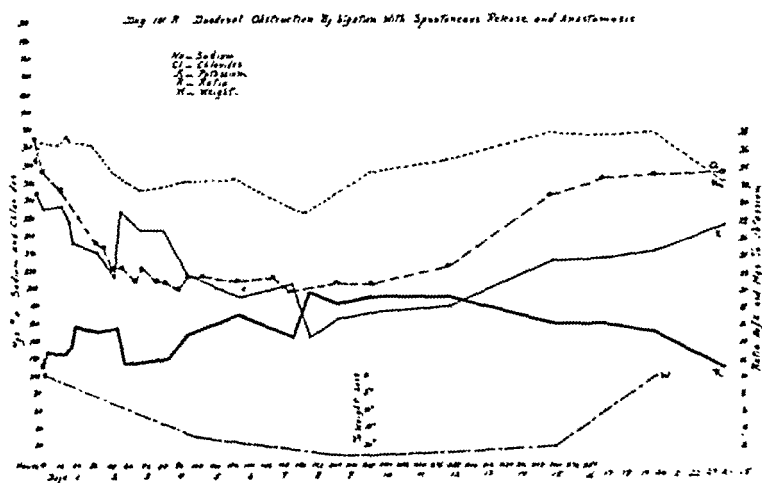


Fig. 7.—Duodenal obstruction with recovery. After becoming moribund, this animal recovered. The ligature had cut through and an end-to-end anastomosis had been established spontaneously. Note that the serum potassium as well as the sodium and chlorides decreased progressively until the animal began to recover. After taking water on the sixth day, there was a sudden drop to very low levels, presumably the result of dilution. Note that the potassium increased more slowly than sodium and chlorides during recovery.

decreased from a preoperative level of 25 to 20 mg. per cent. (See Fig. 8A and B and Protocols 6 and 7.)

It should be noted that in these animals in which strangulation was superimposed upon obstruction and in which death occurred early the serum potassium never became elevated above the normal preoperative levels.

#### DUODENAL FISTULAS

In 2 dogs the duodenum was divided, except for a small bridge of tissue at the mesenteric border, approximately 8 cm. below the ampulla of Vater, and the free margins of both ends were sutured to the skin. Lost through the fistula were not only all of the gastric, biliary, pan-

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Fig. 11. *Strangulation Obstruction By Ligature With Spontaneous Resection and Anastomosis*

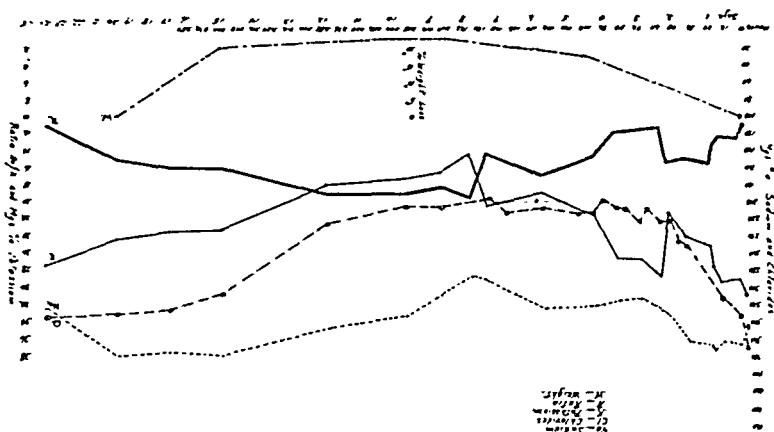


Fig. 7.—Duodenal obstruction with recovery. After becoming moribund, this animal was recovered. The ligature had cut through and an end-to-end anastomosis had been established spontaneously. Note that the serum potassium as well as the sodium and chlorides decreased progressively until the animal began to recover. After taking water on the sixth day, there was a sudden drop to very low levels, presumably the result of dilution. Note that the potassium increased more slowly than sodium and chlorides during recovery.

decreased from a preoperative level of 25 to 20 mg. per cent. (See Fig. 8, I and II and Protocols 6 and 7.) It should be noted that in these animals in which strangulation was superimposed upon obstruction and in which death occurred early the serum potassium never became elevated above the normal pre-operative levels.

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Dog 401R, female; weight, 7.3 kilo.

DUODENAL OBSTRUCTION BY SIMPLE LIGATION  
Protocol 5

HOURS POST-OPERATIVELY	REMARKS	RECTAL TEMPERATURE	CHLORIDES		SODIUM		POTASSIUM	
			SERUM	WHOLE BLOOD	SERUM	WHOLE BLOOD	SERUM	WHOLE BLOOD
24	Vomited several times; weak and dry standing; listless; wobbles when Seum over eyes; Generalized twitching; No definite change; possibly stronger	101.2	331		386		30.2	
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76		101.9	238		360	198	21.8	24.8
90	From this time on the animal improved and rapidly regained normal health. At a subsequent post-mortem examination, it was found that a spontaneous anastomosis had been established around the point of obstruction.	101.5	221		326		21.8	28.9
		100.8	244		365	219	20.8	26.5

SURGERY



per cent from preoperative levels of 26.8 and 22.2 mg. per cent. The chlorides decreased progressively to very low levels as in the ob-

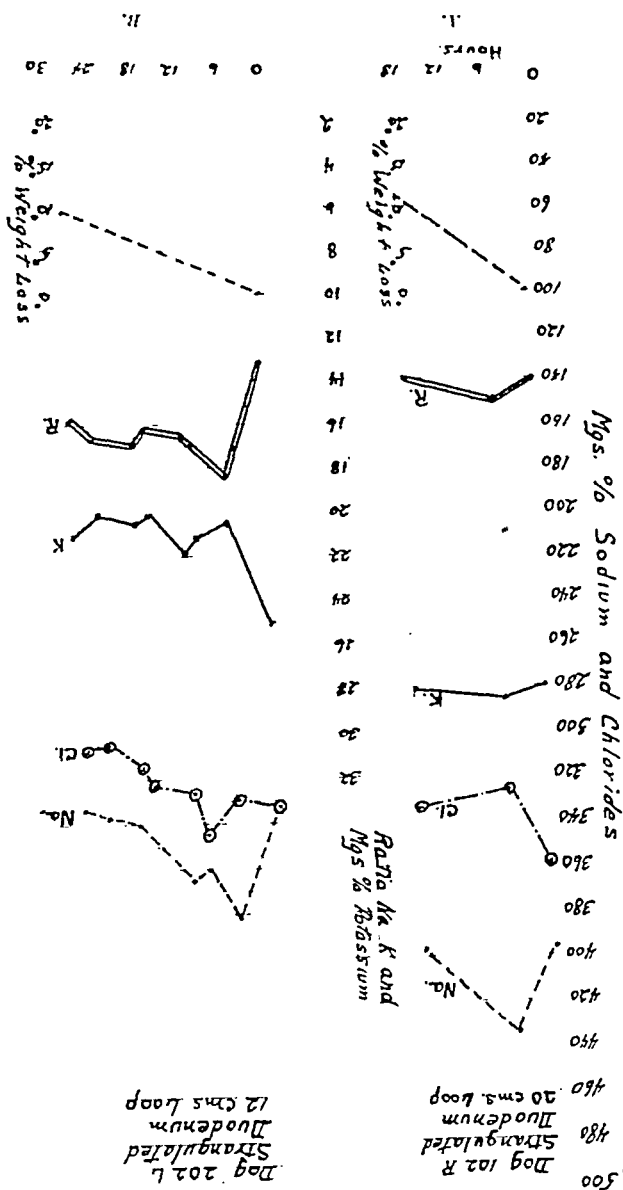


Fig. 8A and B.—Duodenal obstruction with strangulation. Despite profound toxemia with early death, there developed no appreciable alterations in the levels of either sodium, potassium or chlorides.

strangled animals, and sodium showed no consistent or significant change. The sodium-potassium ratios roughly followed inversely the fluctuations of potassium. See Fig. 9A and B and Protocols 8 and 9.

stimulate the sympathetic nervous system, causing a rise in blood pressure. The most important of these pressor bases are isoamylamine, derived from leucine; tyramine, derived from tyrosine; and phenylethylamine, derived from phenylalanine. There are also amines derived from amino acids in the process of putrefaction of protein which stimulate nonstriated muscle and constrict arterioles, even though causing a fall in blood pressure. The most important of these bases is histamine, derived from histidine.

All of these amines are derived from cyclic amino acids of proteins by the process of decarboxylation (loss of  $\text{CO}_2$ ). It is a debated question whether or not autolysis of protein, unaided by bacteria, can produce these amines. They have all been found in putrid protein material and the general belief is that bacteria are essential for their formation. Furthermore, it has been reported (Hanke and Koessler<sup>6</sup>) that certain strains of bacteria will specifically decarboxylate histidine to form histamine, while others decarboxylate tyrosine to form tyramine, but the same strain will not do both. We believe this observation offers a satisfactory explanation for the observation that dog liver incubated without contamination by extraneous bacteria results in the production of pressor amines (tyramine), while dog liver incubated with contaminating bacteria sometimes contains only substances which depress the blood pressure (histamine). We believe that the nature of toxic amines, whether they are histamine- or tyramine-like in character, depends upon the strains of bacteria acting upon the liver substance. In our experience, a more marked toxemia and shock is caused by incubated liver containing a preponderance of histamine and other substances which depress the blood pressure.

Our experiments have demonstrated that putrefactive amines and possibly other heat-stable substances produced by the action of bacteria upon liver in vitro are very toxic. The supernatant fluid from 200 to 300 gm. of incubated liver killed an anesthetized animal when it was given intravenously. When the supernatant fluid from only 100 gm. of incubated liver was given intravenously to a dog without anesthesia, it caused immediate death. The terminal event was marked by convulsive seizures.

When bacteria act upon protein material outside the gastrointestinal tract, they may produce these toxic substances which enter the general circulation without being detoxified by the intestinal mucosa and liver. We believe that this is probably what occurs when either liver material containing bacteria or incubated, autoclaved liver containing the products of bacterial digestion are placed intraperitoneally in the dog. We believe that these water-soluble, heat-stable toxins are important factors which contribute to rapid death in so-called "liver peritonitis." There are other factors which also contribute to rapid

liver intravenously. The sixth dog was given only the supernatant fluid fraction intraperitoneally. The results of the experiment are given in Table I.

TABLE I

THE EFFECT OF SUBJECTING DOGS TO SIMULTANEOUS INTRODUCTIONS OF AUTOCLAVED, FRESH, GROUND DOG LIVER AND THE SUPERNATANT FLUID FROM DOG LIVER, INCUBATED SEVENTY-TWO HOURS, AND STERILIZED BY AUTOCLAVING

DOG	PROCEDURE	RESULT
64	One hundred grams of autoclaved, fresh dog liver were placed intraperitoneally; at the same time the animal was injected intraperitoneally with the supernatant fluid from 100 gm. of dog liver, incubated seventy-two hours, and sterilized by autoclaving	Died in 40 to 44 hr.
65	Same as Dog 64	Died in 32 hr.
66	One hundred grams of autoclaved, fresh dog liver were placed intraperitoneally; at the same time the animal was injected intravenously with the supernatant fluid from 100 gm. of adult dog liver, incubated seventy-two hours, and sterilized by autoclaving	Died in 14 hr.
67	Same as Dog 66	Died in 16 hr.
68	One hundred grams of autoclaved, fresh dog liver were placed intraperitoneally	Survived
69	The supernatant fluid from 100 gm. of adult dog liver, incubated seventy-two hours and sterilized by autoclaving were placed intraperitoneally	Survived

The table shows that neither the autoclaved fresh liver nor the supernatant fluid from incubated liver sterilized by autoclaving caused death. This confirms observations we have made a number of times. When, however, the supernatant fluid from autoclaved, incubated liver containing heat-stable toxic substances is given either intraperitoneally or intravenously to an animal subjected to intraperitoneal implantation of autoclaved fresh dog liver, death results. The experiment indicates that death occurs more rapidly when the supernatant fluid from incubated liver is given intravenously. We can offer no conclusive explanation for this result. However, following intraperitoneal implantation of the toxic amines, it is logical to assume that a certain amount would be deaminized by the liver. Furthermore, it is possible that the autoclaved, fresh liver substance adsorbs part of the toxic material in the supernatant fluid and delays peritoneal absorption so that the life of the animal is prolonged.

The experiment indicates that death of the animals was probably due in part to shock caused by irritation and loss of fluids intraperitoneally. Intraperitoneal absorption of liver protein plus the introduced heat-stable toxins produced in incubated liver were also important factors in causing rapid death.

#### DISCUSSION

It has been recognized for a number of years that among the products of protein putrefaction are several amines that have marked power to

5. It is conceivable that deep-seated infections in human subjects may give rise to toxic amines which enter the general circulation and contribute to the shock syndrome frequently associated with such infections.

We wish to express our appreciation to Dr. W. D. Gatch, under whose supervision our investigations originated.

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death. The intraperitoneal absorption of liver protein per se is associated with the loss of fluids intraperitoneally and toxic degeneration of liver, kidney, and adrenal glands.

Dvorak<sup>7</sup> reported that the Berkefeld filtrate of incubated dog liver caused rapid death of the experimental animal when injected intravenously in amounts equivalent to 4 gm. of incubated liver per kilogram of the animal's weight. We have confirmed this observation. However, we also observed that when the filtrate is autoclaved and then placed intraperitoneally it was equally as toxic as when unautoclaved. On the contrary, when the coagulated proteins were removed from the autoclaved Berkefeld filtrate and the resulting preparation placed either intraperitoneally or intravenously, the animal survived. Apparently autoclaving the Berkefeld filtrates rendered them less toxic. This result could have been due to the coagulation and removal of soluble proteins, the destruction of volatile amines, or the destruction of heat labile bacterial exotoxins. We reported<sup>8</sup> that bacteria isolated from the liver and muscle of normal dogs produced no demonstrable exotoxins. However, more or less specific bacterial endotoxins may be important factors contributing to rapid death in liver peritonitis. We are investigating these factors further.

In this paper we have demonstrated that bacteria found in normal adult dog liver rapidly produces toxic amines in the process of incubation in vitro. It is possible that the rapid death of dogs subjected to liver peritonitis can be adequately explained by shock associated with the absorption of putrefactive amines and other split protein products produced by bacterial action on the liver protein in vivo.

#### CONCLUSIONS

1. The putrefactive pressor bases, tyramine, isoamylamine, phenol-ethylamine, and histamine-like substances, are rapidly produced by the action of bacteria upon liver substances during the process of incubation.

2. Whether or not the amines with pressor effects upon the blood pressure predominate over the amines with depressor effects depends upon the kind of bacteria present in the digests.

3. These toxic amines and other heat-stable, water-soluble, toxic substances formed in the process of incubation of dog liver were lethal when the equivalent of 200 to 300 gm. of incubated liver was given slowly intravenously to an anesthetized dog. When injected intravenously into a dog without anesthesia, the equivalent of 100 gm. of incubated liver was sufficient to cause rapid death. The terminal event is convulsive seizures.

4. We have shown that, in addition to other factors, putrefactive amines may also contribute to the rapid death of dogs subjected to liver peritonitis.

mately sixteen years and indicated a definite advancement of epiphyseal union. The basal metabolic rate was minus 4 per cent and the blood cholesterol was 171 mg. per hundred cubic centimeters of blood. The Wassermann and Kahn tests gave negative reactions. Examination of the blood showed 4,300,000 red cells, 6,400 white cells, and 78 per cent hemoglobin. Examination of the urine revealed no abnormalities except a faint trace of albumin. The blood sugar was 118 mg. per hundred cubic centimeters three hours postprandial.

A diagnosis of virginal hypertrophy of the breasts with probable adenofibromatous change was made, and bilateral simple mastectomy was advised. In view of the child's age and the size of the breast tumor, it was thought advisable to remove the breasts at two separate operations.

At the first operation, the left breast was removed through a transverse incision which surrounded the nipple elliptically and was carried from the axilla to the sternum. The veins overlying the breast were dilated, but bleeding was easily controlled. The breast consisted of a single, lobulated encapsulated mass of firm, adenomatous-appearing tissue which shelled out of the surrounding tissue easily by blunt dissection. Inasmuch as there was no palpable enlargement of the axillary nodes, the axilla was not disturbed and the muscles were not removed. Three days later a similar procedure was carried out on the other side. The patient stood both operations very well and was discharged from the hospital on the sixth day following the last operation. Both wounds were well healed at this time.

The pathologist recorded the weight of the tissue removed at 3,650 gm. for the left breast, and 2,115 gm. for the right breast. Expressed in pounds the left breast weighed just over 8 pounds and the right breast under 4.7 pounds. The total weight of the tissue removed, therefore was nearly 13 pounds, or approximately one-tenth the patient's body weight. On neither gross nor microscopic examination could any normal breast tissue be identified.

The microscopic examination showed an encapsulated tumor consisting of well-differentiated connective tissue, some of which was quite dense and hyalinized and some of which was very loosely arranged and edematous. Irregularly distributed throughout, there were small and large duct or glandlike spaces lined by cuboidal or low columnar epithelial cells, which had no systematic arrangement. A section which was expected to be nontumorous breast tissue showed loosely arranged fibrofatty tissue, but no epithelial elements. An assay for estrin was made of the tissues removed, but no estrogenic substance was found in this material.\*

#### LITERATURE

McFarland<sup>4</sup> emphasizes the difficulty of making a histologic differentiation between fibro-adenoma of the breast and normal breast tissue. Of 289 cases which were supposed to be benign, fibro-epithelial tumors, 147 were, on closer analysis, shown not to be tumors as had been reported by the pathologist, but to be either normal breast tissue or breast tissue in some normal phase of involution or hyperplasia. McFarland's conclusion shows the close relationship which exists between fibro-epithelial tumors of the breast and normal breast tissue and raises the question of the influence of the sex hormones on the formation and development of fibro-epithelial tumors.

\*The estrin assay on the breast tissue was made by grinding up the fresh tissue and extracting with benzol.

# LARGE BILATERAL ADENOFIBROMAS OF THE BREAST

## REPORT OF CASE IN A GIRL THIRTEEN YEARS OF AGE

GEORGE CRILE, JR., M.D., CLEVELAND, OHIO

*(From the Cleveland Clinic)*

ALTHOUGH the literature contains several reports of enormous adenofibromas of the breast in young girls, this condition is sufficiently rare to warrant the report of an additional case in which large bilateral adenofibromas of the breast, the larger of the two weighing eight pounds, were present in a girl thirteen years of age.

### REPORT OF CASE

The patient was a girl, thirteen years of age, whose development had been perfectly normal until one year before entry. At that time her breasts began to enlarge, but the development appeared to be normal for her age. Eight months before entry, the breast development had become more marked than the family thought was normal, and the breasts continued to enlarge rapidly and painlessly and became pendulous and burdensome. There was never any discharge from the nipples.

The patient had not menstruated and there was no pubic hair or other evidence of secondary sexual characteristics. During the year preceding our examination, she had gained four inches in height and thirty-five pounds in weight. The family history contained no data relevant to the illness.

Physical examination showed a fairly tall child, the height being sixty-six inches and the weight 125 pounds. She was slightly pale, but appeared to be in good health. There were some dental caries; the tonsils had been removed; the thyroid gland was not enlarged or tender; the heart and lungs showed no abnormality. Rectal examination of the pelvic organs showed no adnexal masses and the uterus, which was infantile, could scarcely be palpated. There was an enormous, nodular enlargement of both breasts (Figs. 1 and 2). They were firm, rounded, and pendulous, hanging to a point well below the umbilicus. The nipples were flattened out and practically invisible. There were many dilated veins over the breasts. Nodular, firm, breast tissue could be palpated well out into the axillae up nearly as high as the clavicles and medially nearly to the sternum.

In view of these unusual findings and in an effort to determine whether there was any endocrine basis for the abnormality of the breasts, a qualitative prolan assay was done by McCullagh's modification of the Friedman test.<sup>1</sup> Urinary estrin was extracted quantitatively with benzol by Koch's method<sup>2</sup> and assayed by a modification of Kurzrok's method,<sup>3</sup> in which variations range from 4.5 to 20 rat units in normal adult women. The Friedman test gave negative findings. An assay for estrogenic substance in two twenty-four-hour specimens of urine showed 26.4 rat units in 1,425 c.c. of urine and 17.6 rat units in 940 c.c. respectively, figures which, by the method of assay used, are within normal limits for adult women. Roentgen examination of the epiphyses at the elbow and hip showed a bone age of approxi-

mately sixteen years and indicated a definite advancement of epiphyseal union. The basal metabolic rate was minus 4 per cent and the blood cholesterol was 171 mg. per hundred cubic centimeters of blood. The Wassermann and Kahn tests gave negative reactions. Examination of the blood showed 4,300,000 red cells, 6,400 white cells, and 78 per cent hemoglobin. Examination of the urine revealed no abnormalities except a faint trace of albumin. The blood sugar was 118 mg. per hundred cubic centimeters three hours postprandial.

A diagnosis of virginal hypertrophy of the breasts with probable adenofibromatous change was made, and bilateral simple mastectomy was advised. In view of the child's age and the size of the breast tumor, it was thought advisable to remove the breasts at two separate operations.

At the first operation, the left breast was removed through a transverse incision which surrounded the nipple elliptically and was carried from the axilla to the sternum. The veins overlying the breast were dilated, but bleeding was easily controlled. The breast consisted of a single, lobulated encapsulated mass of firm, adenomatous-appearing tissue which shelled out of the surrounding tissue easily by blunt dissection. Inasmuch as there was no palpable enlargement of the axillary nodes, the axilla was not disturbed and the muscles were not removed. Three days later a similar procedure was carried out on the other side. The patient stood both operations very well and was discharged from the hospital on the sixth day following the last operation. Both wounds were well healed at this time.

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The microscopic examination showed an encapsulated tumor consisting of well-differentiated connective tissue, some of which was quite dense and hyalinized and some of which was very loosely arranged and edematous. Irregularly distributed throughout, there were small and large duct or glandlike spaces lined by cuboidal or low columnar epithelial cells, which had no systematic arrangement. A section which was expected to be nontumorous breast tissue showed loosely arranged fibrofatty tissue, but no epithelial elements. An assay for estrin was made of the tissues removed, but no estrogenic substance was found in this material.\*

#### LITERATURE

McFarland<sup>4</sup> emphasizes the difficulty of making a histologic differentiation between fibro-adenoma of the breast and normal breast tissue. Of 289 cases which were supposed to be benign, fibro-epithelial tumors, 147 were, on closer analysis, shown not to be tumors as had been reported by the pathologist, but to be either normal breast tissue or breast tissue in some normal phase of involution or hyperplasia. McFarland's conclusion shows the close relationship which exists between fibro-epithelial tumors of the breast and normal breast tissue and raises the question of the influence of the sex hormones on the formation and development of fibro-epithelial tumors.

\*The estrin assay on the breast tissue was made by grinding up the fresh tissue and extracting with benzol.



Cheatle<sup>5</sup> states that fibro-adenomata of the breast may be either localized tumors or that they may take the form of a diffuse fibro-adenomatosis affecting the whole breast. He believes there is no difference between the localized and diffuse form in either gross or microscopic appearance. Since fibro-epithelial tumors of the breast so closely resemble normal breast tissue, it is not unreasonable to assume that various endocrine disorders which affect normal breast tissue could likewise play a part in the formation and development of fibro-epithelial tumors of the breast.

Lewis and Geschickter<sup>6</sup> state that they were able to produce changes in the breasts of male monkeys by the injection of estrin in amounts

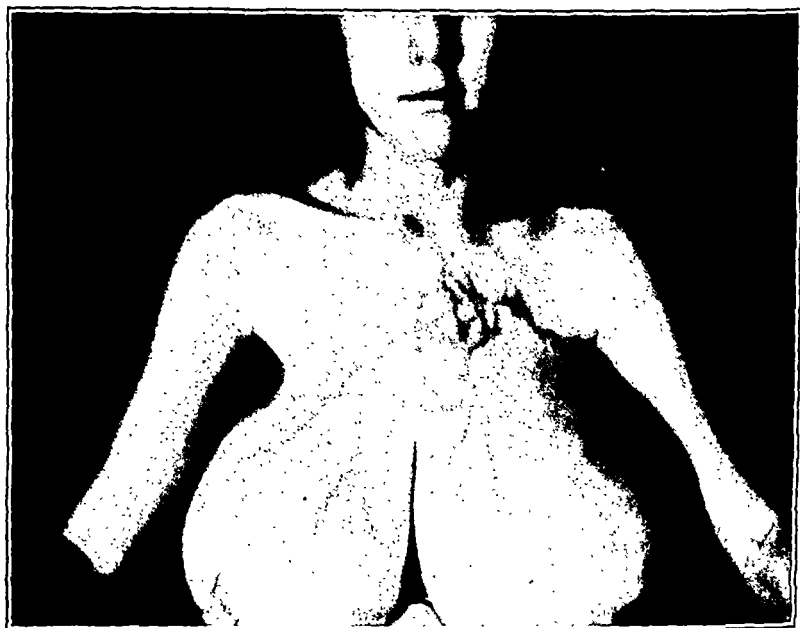


Fig. 1.—Dilatation of veins shown by infra-red technique.

varying from 2,000 to 5,000 rat units. These changes resulted in a condition resembling, but not identical with, gynecomastia. The length of the ducts was increased, the ducts dilated, and there was an increase in the number of epithelial layers. These workers state that there is much clinical evidence to support the view that gynecomastia is due to the action of estrin and quote the case reported by Heidrick in which gynecomastia was associated with a teratoma of the testicle which had resulted in the production of 250 units of the female sex hormone and 3,500 units of gonadotropic hormone per liter of urine. According to Lewis and Geschickter, a localized response of the breast to endocrine disorders leads to the formation of fibro-adenoma, while a general response in one or both breasts causes unilateral or bilateral

virginal hypertrophy. According to these authors this accounts for the clinical fact that fibro-adenomas and virginal hypertrophy are frequently associated.

From their microscopic studies, Lewis and Geschickter<sup>6</sup> believe that the formation of fibro-adenomata is essentially an exaggeration of puberty hypertrophy, that fibro-adenomas, gynecomastia, and virginal hypertrophy may represent different phases of the same process, and



Fig. 2.—Lateral view showing flattening of nipple.

that their development might be dependent upon ovarian hormones. They report the case of a large fibro-adenoma in a twelve-year-old colored girl who had not yet menstruated.<sup>7</sup> The fibro-adenoma contained large quantities of estrin, there being 2,500 units per pound of tissue. Lewis and Geschickter believe these findings indicate that the type of tumor tissue under discussion has a marked capacity to concentrate estrin.

Although the development of large fibro-adenomata of the breast in girls or young women is unusual, a number of cases similar to the

one presented here have been reported. Turner<sup>8</sup> reports two cases of multiple, rapidly growing, soft fibro-adenomata of the breast, one in a girl fifteen years of age and the other in a girl fourteen years of age. In both cases the enlargement commenced at or just after puberty. In both, the enlargement was rapid and excessive and was due to the presence of multiple soft fibro-adenomata. In one case the tumor was unilateral and in the other bilateral tumors were present. Unfortunately no histologic examination was made in the first case, but in the second case the histologic report confirmed the clinical and gross pathologic diagnosis of fibro-adenomata of the breast. The weight of the tumors in both breasts in the fourteen-year-old girl was 15½ pounds. The left breast was larger and weighed 8 pounds immediately after its removal. It is interesting to note that in this case regular menstruation had not been established prior to the removal of the breast tumor. The patient had menstruated once eight months before admittance to the hospital and following this the breasts had begun to enlarge and she had not menstruated again. During this time she had become undernourished and wasted. It is also interesting to note that no normal breast tissue could be recognized. In the first case, that of the fifteen-year-old girl, the patient had menstruated for nearly one year. Only one breast was involved. Three years after the removal of the right breast, a fibro-adenoma developed on the left side and it was necessary to excise the left breast also.

Sellers<sup>9</sup> reports a case of an unusually large fibro-adenoma of the breast in a twelve-year-old colored girl in whom menstruation had not begun. Enlargement of the breast was first noted about three months before entry. The left breast was greatly enlarged and the skin tightly stretched. The overlying veins were dilated, but there was no fixation of the tumor nor were any axillary nodes palpable. A radical mastectomy was performed. The pathologic report was fibro-adenomata of the breast. The weight of the tumor was not given. Later it was necessary to excise a fibro-adenoma of the right breast as well.

Beatson<sup>10</sup> reports a fibro-adenoma of the right breast in a married woman fifty years of age. The tumor weighed six and one-half pounds and had been developing for over a period of two years.

Finsterer<sup>11</sup> reported a fibro-adenoma of the breast in a single woman forty-five years of age. The weight of the breast including the axillary fat was 4½ kg.

Barton<sup>12</sup> described a large fibro-adenoma of the breast in a colored girl seventeen years of age. The weight of the specimen was not given, but the breast measured twenty-seven inches in circumference.

The largest fibro-adenomatous hypertrophy of the female breast which I could find reported in the literature was described by Touraine

and Renault.<sup>13</sup> In this case there was a massive bilateral hypertrophy of the breast with fibro-adenomatous changes. The patient was thirty-six years of age and the enlargement of the breast had begun six years previously, immediately following the removal of the right tube and ovary. The total weight of the tissue removed was 9 kg., 150 gm., or approximately 19.7 pounds.

#### DISCUSSION

It is clear from this survey of the literature that large fibro-adenomas of the female breast may develop at any age from before puberty to the menopause and in married women as well as in unmarried women. These tumors are frequently difficult to differentiate, either clinically or by microscopic examination, from the so-called virginal hypertrophy. Although no definite etiologic factors have been demonstrated, it is possible that endocrine disturbances play a part in their development.

The case reported in this paper is unusual as regards the size of the tumor and the youth of the patient.

As McFarland<sup>4</sup> has shown, it is often difficult to determine by microscopic examination whether a section from the breast is breast tissue in a normal state of physiologic hyperplasia or involution, or whether it is a true fibro-epithelial tumor. The presence or absence of a true fibro-epithelial tumor should be determined by gross examination but, in the case reported here, even the gross examination did not conclusively prove whether or not the breast changes were the result of extreme hypertrophy or were caused by the development of bilateral fibro-epithelial tumors. The fact that the masses were well encapsulated, lobulated, and had the gross appearance of a tumor is in favor of their being true adenofibromas, but against this hypothesis is the fact that no normal breast tissue could be identified.

#### CONCLUSIONS

1. A case of enormous bilateral adenofibromatous tumors of the breasts occurring before puberty in a girl thirteen years of age is reported. The weight of the left breast was 8 pounds and of the right 4.7 pounds.

2. Assays of the urine showed estrogenic substance in amounts equivalent to that found in normal adult women.

3. Assays of the tumor tissue were negative for estrogenic substance.

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# STENOSIS OF THE LARGE BOWEL DUE TO AMEBIASIS

## REPORT OF A CASE TREATED BY EXTENSIVE RESECTION

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DESPITE the incidence of amebiasis and the undoubtedly frequent occurrence of severe damage to the colon, the surgical literature contains but few instances of extensive colonic resections in these cases. Chatterji<sup>1</sup> says that in rare cases of ulceration of the cecum it may be necessary to excise the cecum and perform an enteroanastomosis. Yeomans<sup>2</sup> reported the case of another surgeon where the transverse colon and splenic flexure were resected for amebic granuloma. This patient died two days later. In Huard's<sup>3</sup> careful presentation of the surgical aspects of cecocolonic amebiasis, no reference to colonic resection could be found.

The following case report is of interest because of the widespread damage to the colon and because of the improvement following radical excision combined with medical treatment.

CASE REPORT.—S. P., aged fifty-four years, male, was admitted to the Evanston Hospital on April 28, 1935. He had been under the care of J. M. Garner for a lobar pneumonia since April 10, 1935. About April 21, the patient developed epigastric pain which soon became localized in the right lower quadrant. This was accompanied by gaseous distention and diarrhea. Meanwhile the pneumonia showed definite resolution after April 17. The patient appeared quite ill, and the chief physical finding was a tender mass in the right lower quadrant about four inches in diameter. The temperature was 100° F.; the pulse, 100; and the respirations, 26. The leucocyte count was 37,900; the erythrocyte count was 5,410,000 and the hemoglobin was 102 per cent. The urine was negative. Three stools, examined on April 29 and 30, were negative for amebas, but showed a trace of occult blood.

On April 30, 1935, the mass in the right lower quadrant was explored under the impression that it was an appendiceal abscess. A rather large inflammatory mass involving the cecum was found and an abscess was located above the ileocecal valve and on the posterior mesial aspect of the colon. The abscess was drained after the evacuation of thick green ill-smelling pus. The wall of the cecum at this point seemed to be very friable; in fact, partially necrotic. On May 2, 1935, a definite fecal fistula was established at the abdominal wound. Amebas were found in the discharge from the fecal fistula. The patient had a prolonged and difficult convalescence featured by a period of pyrexia, chills with attention directed to the chest, and an amebic ulceration of the wound borders requiring excision under gas. On May 10 to 12, large ill-smelling necrotic sloughs were passed by rectum. The patient was given two courses of vioform (grains III t.i.d.), from May 17 to 26 and from June 2 to June 21. On June 19, 1935, a proctoscopic examination

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(C. E. Pope) disclosed a tubular stricture 7.5 cm. from the anus with total denudation of the mucosa. The patient was discharged from the hospital on June 21, 1935, with a draining fecal fistula but improved in general health.

During the summer months, the patient had considerable difficulty with an exacerbation of the amebiasis, which was treated by a course of emetine, painful excoriation of the wound borders, and arthritis of the left arm and leg. The patient was readmitted to the Evanston Hospital on September 12, 1935. There was now a complete stenosis of the proximal portion of the rectum and the patient experienced considerable pain when the large bowel filled with gas. The erythrocyte count was 4,440,000 and the hemoglobin was 90 per cent. The urine was negative and the stools were negative for amebas.

Laparotomy was carried out on September 13, 1935. At operation (through a left rectus incision) the entire ascending colon, transverse colon, splenic flexure, and most of the descending colon was found to be atrophied down to a hard cord about  $\frac{1}{4}$  to  $\frac{1}{2}$  inch in diameter and was apparently devoid of lumen. The sigmoid flexure from the upper end of the rectum to a point half-way up the descending colon, a distance of about 10 inches, was normal. The terminal ileum was implanted, end-to-side, into the most proximal portion of the normal sigmoid flexure. The most distal portion of this sigmoid flexure was then brought out through the lower angle of the wound and the peritoneum and fascia were sutured beneath the loop. Last of all a mushroom catheter was placed by purse-string in the exteriorized colostomy loop. The patient was discharged from the hospital on September 27, 1935, in good condition with a well-functioning left inguinal colostomy and some discharge from the old cecostomy.

The patient was readmitted to the Evanston Hospital on November 21, 1935. His chief complaint was now a severe arthritis, involving the hands, feet, elbows, and shoulders, of some three months' standing. The erythrocyte count was 5,590,000; the hemoglobin, 110 per cent, and the leucocyte count, 10,200. The urine was negative and the stools were negative for amebas. X-ray examination after oral administration of barium showed that there was not complete occlusion of the colon at any point proximal to the sigmoid. The lumen of the transverse colon, however, was narrowed to about  $\frac{1}{4}$  of 1 inch in diameter. The cecum and a portion of the ascending colon also were involved in the contracting process. The stricture between the sigmoid and rectum would not permit the passage of barium.

On November 29, 1935, the patient was again subjected to laparotomy. The transverse colon was found to be narrowed almost to a cord. This narrowing was also present in the ascending colon save for a small portion near the hepatic flexure. The terminal ileum, appendix, cecum, ascending colon, and transverse colon were entirely removed closing the upper descending colon just above the previously performed ileocolostomy. The excised specimen showed chronic ulcers, but no amebas were found in the stained sections. The patient recovered from this operation very satisfactorily and left the hospital on December 10, 1935.

After leaving the hospital, Garner gave the patient a course of sodium cacodylate, as well as an autogenous vaccine. The patient gradually improved and the swelling and pain in the joints subsided. A diet rich in vitamins and parenteral liver extracts was given. In May, 1937, the patient weighed 185 pounds, a gain of 100 pounds from his lowest weight in the hospital. The cecostomy wound had healed entirely. He is now working five hours a day at home and is able to drive his car. He walks around the block three times a day. He still has pain in his joints which diminishes, however, during the day. The colostomy functions well.

The patient takes a heaping teaspoonful of kaolin four times a day and paregoric occasionally. The stools are fluid in the morning but soft in the evening. He changes the colostomy dressing four times daily.

#### SUMMARY

A case of widespread damage to the colon from amebiasis is reported. The resultant stenoses and structures were successfully treated by extensive resection of the colon with ileosigmoidostomy plus external sigmoidostomy.

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Difficulty in breathing immediately after birth should always suggest the possibility of a defect in the diaphragm. This symptom may moderate after a few days only to reappear in a few weeks or months. Also, there will usually be difficulty with feeding, and failure to gain weight normally. The chief physical signs are small abdomen, displacement of the heart, and absence of breath sounds over the affected side. These findings should suggest x-ray examination with the barium meal, which will definitely establish the diagnosis.

One of the most troublesome technical difficulties in the surgical repair of these cases is the closure of large defects. I have been impressed with this on the two occasions that I have performed the operation. In my first experience, there was a large posterolateral defect on the left side, apparently a persistent pleuroperitoneal canal. An attempt to approximate the edges of the ring was unsuccessful. After placing the abdominal viscera outside of the abdomen to allow more complete exposure of the defect, the renal fascia presented itself as a broad expanse of firm tissue which might be utilized as an aid in accomplishing the closure. By grasping it with forceps it was possible to displace it for a considerable distance cephalad and ventrad and thus attach it to the anterior margin of the defect without undue tension. Since then it has come to my attention that Barrett and Wheaton<sup>7</sup> had previously recommended the use of the renal fascia in the closure of these defects, and from personal communications it would appear that others have also made use of it. That the closure of large defects is often difficult to accomplish is evident from the radical procedures which have been required in some instances. In two successful cases, Bettman found it necessary to fracture the lower ribs and change the convexity of the thoracic wall to a concavity in order to effect a closure. Studies which have been made of the renal fascia indicate that it may, at times, be of inestimable value in this connection and for this reason one who undertakes the repair of a large defect should have a complete knowledge of its possibilities. The mobility and expanse of this tissue is sufficiently great to permit closure of large defects even to the degree of complete absence of a hemidiaphragm.

#### ANATOMY OF THE RENAL FASCIA

This fascia is a continuation of the sheath of the psoas major muscle and the arcuate ligament. After leaving the muscle, it extends laterally and downward, its anterior layer covering the anterior surface of the kidney and adrenal gland. After leaving the kidney, it continues laterally as the fascia of the transversalis muscle. It is somewhat thinner over the region of the kidney and adrenal gland than it is over the psoas muscle, but it is nevertheless a definite firm layer of fascia possessing considerable tensile strength. It is loosely attached to the kidney through fibrous strands in the adipose capsule, and the kidney is largely dependent upon it for fixation in its normal position. When

# DIAPHRAGMATIC HERNIA IN INFANTS; SURGICAL TREATMENT WITH USE OF RENAL FASCIA

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UNTIL very recently, congenital diaphragmatic hernia occurring in infants was not thought to be within the possibility of surgical repair. Hume, writing in 1922, reflected the attitude of the medical profession when he stated that repair of congenital diaphragmatic hernia was not a feasible procedure, and that the most one could hope to accomplish by surgery would be the release of incarcerated or strangulated bowel with no attempt at closure of the defect. Apparently this belief is still widespread, notwithstanding recent successes which prove otherwise.

One of the reasons for the slow development of surgical treatment in the early age group is the erroneous impression that infants do not tolerate extensive procedures within the abdomen or thorax. As a consequence, operations have been withheld until the infants are in extremis, either from intestinal obstruction or from respiratory embarrassment, and attempts at repair have been made under most unfavorable conditions, with very little chance for success. This fault is partly due to the failure to appreciate the difference between defects occurring in infants and those occurring in more mature persons. It is well known that large displacements of intestine into the thorax are occasionally found in individuals living to old age, many of them having no symptoms during life, and being discovered only in routine examination. This has led to the belief that surgical interference should be resorted to only in the presence of severe disturbances of digestion or respiration. This attitude may be acceptable for those making themselves evident after the first years of life, as the changes in this group which indicate surgery are usually slow in their development, and in the early stages of these disturbances the child and adult are better able to withstand the surgical attack. But the situation is quite different in the infant. When it is considered that most cases of congenital diaphragmatic hernia do not live beyond the first few months (Keith,<sup>1</sup> Hedblom,<sup>2</sup> Latta<sup>3</sup>), it is obvious that there must be a different attitude toward this age group. The obstetrician, pediatrician, and surgeon are faced with a situation which requires early recognition and prompt surgical treatment, even in the first few hours of life. The successful cases reported by Johnson<sup>4</sup> on a forty-two-hour-old infant, by Coryllos<sup>5</sup> on a thirteen-day-old infant, and by Orr<sup>6</sup> on a twenty-seven-day-old infant are evidence that early age is not a barrier to operation.

the adrenal gland lies in close proximity to the posterior aspect of the anterior layer, and this relationship must be considered in making use of the fascia in the manner to be described later. Further, congenital diaphragmatic hernia which has existed for more than a few days results in extreme distortion of the normal anatomic relationships. The mesentery of the intestine is stretched considerably and the pedicle of the spleen becomes greatly elongated. Because of the latter distortion one

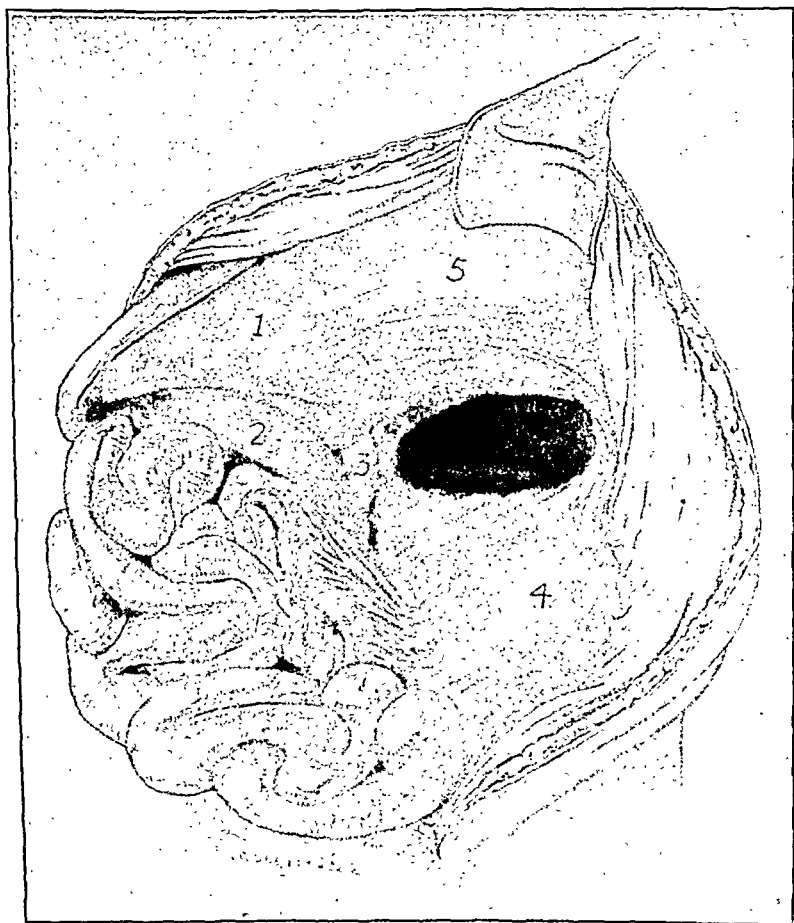


Fig. 2.—Same case as shown in Fig. 1 after displacement of the intestines and spleen from the thorax, showing the defect in the diaphragm and the expanse of renal fascia. 1, Liver; 2, spleen; 3, stomach; 4, renal fascia; 5, diaphragm.

may accidentally ligate the lienal artery in suturing the renal fascia to the anterior border of the defect unless the altered relationships are kept in mind.

#### TECHNIQUE OF OPERATION

The infant is placed in an anterolateral position, with the head down to lessen the possibility of aspiration of stomach contents during the

the fascia is displaced upward, the kidney is elevated with it and by this means may be displaced for a relatively great distance, even into the thorax. As the anterior layer of renal fascia approaches the diaphragm,



Fig. 1.—Diaphragmatic hernia through the left pleuroperitoneal canal in an infant, aged twenty-eight hours. The spleen and most of the intestines are within the left pleural cavity. 1, Liver; 3, stomach; 4, renal fascia; 5, diaphragm.

it fuses with the posterior layer and continues cephalad to unite with the fascia of the diaphragm. There are no important nerves or vessels which are intimately connected with the fascia. However, the artery to

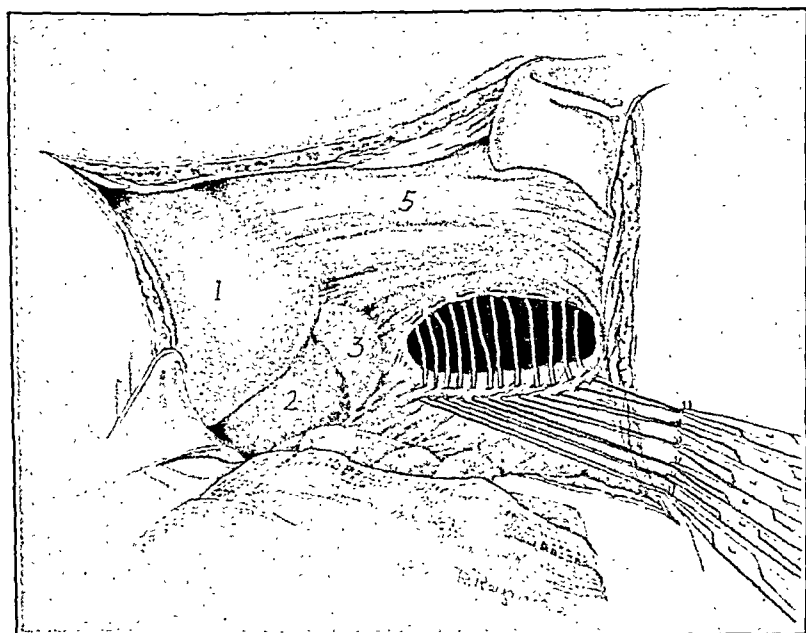


Fig. 5.—Interrupted silk sutures inserted in the anterior border of the hernial ring and in the renal fascia. The intestines, covered with wet gauze, are placed outside of the abdomen.

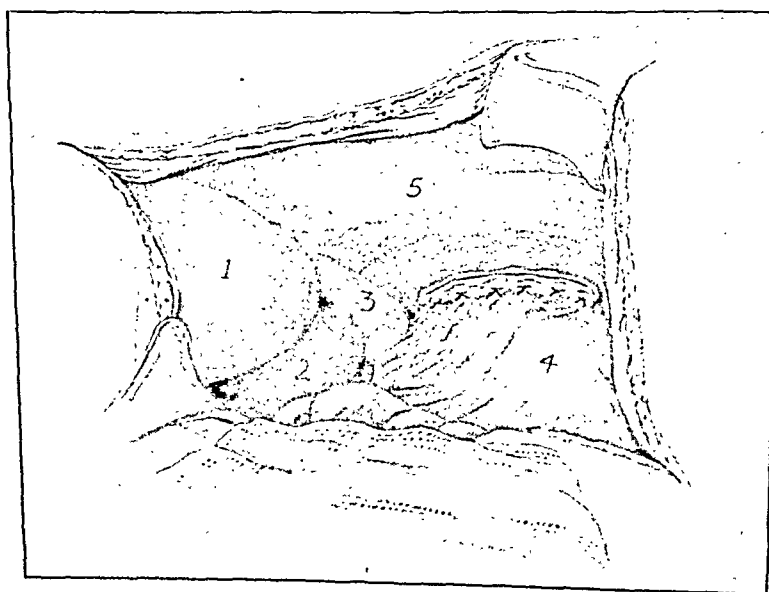


Fig. 6.—Closure of the defect, showing the upward displacement of the kidney which takes place with elevation of the renal fascia.

course of the operation. A lateral abdominal incision is made along the inferior costal margin from the sternum to the longitudinal muscles of the spine. This wide exposure allows full visualization of the defect in the diaphragm which usually lies posterolaterally. As a general rule the spleen and most of the gastrointestinal tract are within the thorax. These structures are displaced by introducing a rubber tube of about

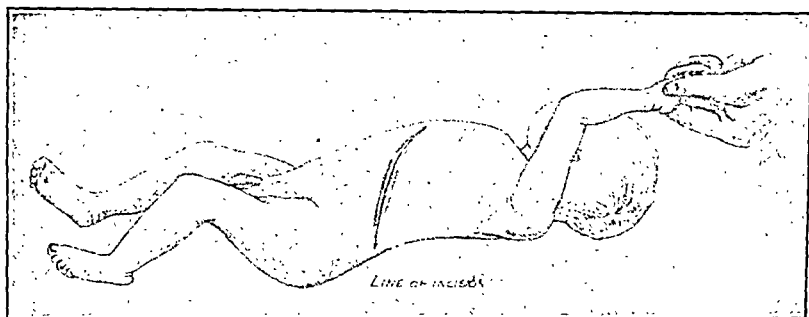


Fig. 3.—Technique of surgical repair, showing line of incision along left costal margin.

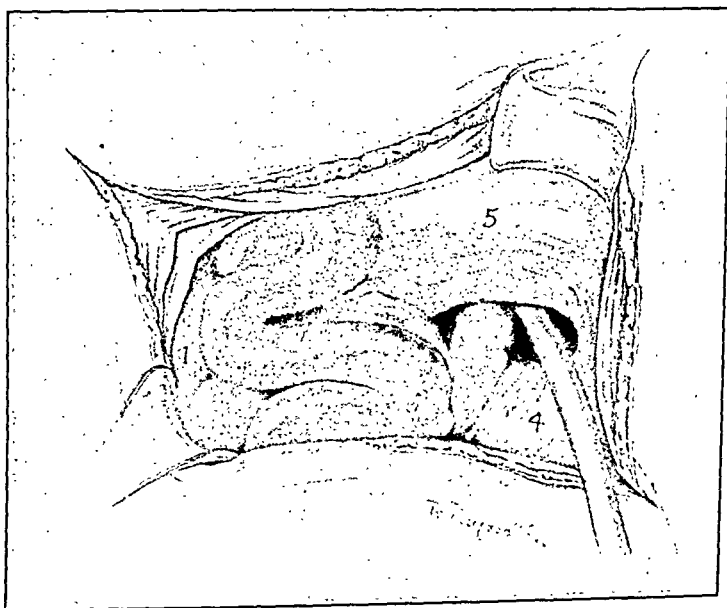


Fig. 4.—Displacement of intestines from the thorax by introduction of rubber tube through hiatus.

$\frac{5}{8}$  inch in diameter through the aperture, a method suggested by C. H. Mayo.<sup>8</sup> One is impressed by the ease with which the intestine passes from the thorax into the abdomen with this simple maneuver, as compared with the difficulty experienced in reducing the hernial contents without it. The air which enters the thorax through the tube is ap-

sure by varying the pressure of the oxygen which is administered with the anesthetic agent. While cases have been operated on successfully without the use of positive pressure anesthesia, it is hazardous to work in the open thorax without this precaution.

#### POSTOPERATIVE CARE

The aftercare is directed chiefly toward restoring the normal body fluids, which have become depleted because of difficulty in feeding, and toward maintaining adequate oxygenation. Oxygen inhalation with carbon dioxide or carbon dioxide alone may be needed in the first few days after operation. Water is usually tolerated by mouth within a few hours. The feedings are increased to normal without long delay as starvation is one of the serious features of the disturbance which must be combated early.

#### COMMENT

The operation should be performed at an ideal time if possible, and one should not wait for symptoms of obstruction or pneumonitis before advising surgical treatment. As stated before, many cases have been operated upon while the infants were in a poor state of nutrition and suffering from toxic disturbances. It is reasonable to assume that the high mortality which has attended the operation up to the present time is due in part to performance of the operation at an unfavorable time.

I have operated on two patients by the method described here. The first, an infant aged five months, was operated upon in February, 1935. In this case there was a large posterolateral defect in the left hemidiaphragm, apparently a persistent pleuroperitoneal canal. Symptoms of dyspnea and difficulty in feeding had been noticed since birth, but the infant had gained weight until three weeks prior to admission to the University Hospital. At that time he appeared to have a slight cold and there was marked effort in breathing. During the following weeks his weight dropped from thirteen pounds eight ounces to twelve pounds five ounces. Examination showed the heart displaced to the right and breath sounds absent over the left hemithorax. This suggested the possibility of a diaphragmatic hernia, and the diagnosis was established by means of x-ray after barium meal. Operation was performed according to the procedure described above, and the patient made an uneventful postoperative convalescence with the exception of a sharp rise in temperature twenty-four hours after operation. This infant has developed into a normal healthy youngster and shows no signs of any disorder. A recent x-ray examination shows return of the structures in the thorax to the normal position and a normal arrangement of the viscera in the abdominal cavity.

The second case operated on by this technique was that of a baby girl aged eight months. She had shown signs of respiratory difficulty since birth and had failed to gain weight normally. During the first



parently all that is needed to overcome the negative pressure induced by respiration, the force which has caused the suction of the intestines into the thorax.

After the abdominal viscera are dislodged from the thorax, positive pressure anesthesia is started, because the aperture which was more or less closed by the herniated viscera up to this time is now widely open and the already embarrassed lungs and heart may be unable to withstand the sudden increase in atmospheric pressure. The abdominal viscera are now placed in gauze soaked in warm normal saline solution, thus leaving the abdominal cavity empty to facilitate inspection and repair of the defect. Small forceps which will give a minimum of trauma are spaced at intervals of about  $\frac{3}{4}$  inch along the anterior border of the hernial ring in order that they may serve as retractors and also aid in approximating the edges of the defect. The broad expanse of renal fascia which now lies completely exposed is grasped with forceps and raised upward to meet the anterior border of the hernial ring. In the case of relatively small defects it will not be necessary to use the renal fascia. If, however, the defects are extremely large, up to complete absence of the hemidiaphragm, it will be necessary to grasp the renal fascia more caudally and raise it cephalad to meet the thickened anterior margin of the diaphragm which may be its only remnant. Interrupted mattress sutures of No. 9 silk are placed sufficiently close together to assure complete approximation of the edges along the line of closure. Fine silk is preferred for several reasons. It is less irritating; it may be used in much finer size than catgut; and it is more durable and thus is more fitted to withstand the tension of the contracted diaphragm. After the sutures are tied, the intestines are returned to the abdomen, placing them as nearly as possible in their normal relationship without more than necessary manipulation and without consuming too much time. After suturing the fascial layers of the abdominal wall with interrupted 0 chromic catgut, the skin is approximated. Before the infant leaves the operating room, air is withdrawn from the pleural cavity by means of an aspirating needle and syringe. This aids the expansion of the lung by reducing the intrapleural pressure.

#### ANESTHESIA .

The anesthesia should be administered by one who understands the disturbances occurring with the open thorax. Because of the already embarrassed respiration, the sudden inrush of air with the opening of the abdomen or thorax is especially liable to cause failure of respiration and one must be prepared to use positive pressure anesthesia whenever this danger threatens. Preliminary local anesthesia followed by the maintenance of a mild degree of ether and nitrous oxide general anesthesia is a satisfactory method when used with the rebreathing bag and positive pressure. It is not necessary to use an elaborate apparatus. A tight fitting face mask permits regulation of the intrapulmonary pres-

## THE EFFECT OF ANESTHESIA ON HEPATIC FUNCTION

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PRIOR to the introduction of methods for determining the status of liver function, the clinician had observed that in the use of certain anesthetics liver damage was to be expected in varying degrees. In 1850, four years after the introduction of chloroform, Casper<sup>1</sup> published reports of cases of death resulting several days after the use of this anesthetic. His observations were later confirmed by others, and during the period from 1850 to 1900 the pathology produced in the liver by anesthetics was thoroughly studied.<sup>2</sup>

Clinical observation, various functional tests, and experimental investigation have demonstrated that certain anesthetics are injurious to the system. A depressed kidney function and a depressed liver function may result from an anesthetic, but this is only an expression of a generalized depression of the cell activity of the organism. The fall in body temperature, which is so well illustrated in the temperature charts of patients following anesthesia, is the reflection of a generalized effect on the body. Oliguria or anuria, depending upon the depth and length of narcosis, is an occasional observation in the surgery ward following the administration of chloroform, ether, and avertin. Following cholecystotomy with drainage externally, the surgeon does not become alarmed if the quantity of bile flow is practically nil the first 24 to 48 hours. Mann<sup>3</sup> in 1925 observed the effect of ether on hepatic activity, stating that it resulted in a hyperglycemia dependent wholly upon the liver and that it depressed the secretion of bile. Barbour and Bourne<sup>4</sup> have shown that ether and chloroform always cause a marked blood concentration. A true acidosis<sup>5</sup> which varies in degrees of intensity is produced by avertin and by the inhalation anesthetics. The percentage of hemoglobin is decreased and there is a slight degree of hemolysis. Chloroform increases the coagulation time of the blood, and nitrous oxide, ether, and ethylene decrease the time of coagulation. The central nervous system manifests effects produced by an anesthetic, varying from the subjective symptoms of inability to think and impairment of memory to that of death resulting from nitrous oxide. From these various effects of anesthesia, it can readily be seen that the liver does not by any means bear the brunt of the damage produced.

In order to determine the effect of anesthesia on hepatic function, it is of importance to consider other factors which might influence that organ, or the determined status of function. First, does operative inter-

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four months of life she was considered to be a case of malnutrition without known cause. Also, a diagnosis of dextrocardia had been made. At the fifth month x-ray examination was made with barium meal because of the possibility of diaphragmatic hernia, and this revealed the presence of the stomach and intestines within the left hemithorax. Because of progressive loss of weight and dyspnea on exertion to a point of danger, operation was decided upon. Several days before operation she had had an attack of what appeared to be temporary obstruction of the intestine, and for this reason operation was considered all the more imperative. At operation it was found that the left hemidiaphragm was almost entirely absent, being represented by a ring of muscle and fascia at the normal site of its attachment, and by a large thin sac extending to the apex of the left hemithorax. Making use of the renal fascia for the posterior border, and the margin of the rudimentary muscle of the diaphragm for the anterior border, the defect was closed by interrupted sutures. In doing so the size of the abdominal cavity was reduced to such a degree that it was difficult to return the intestines to the abdomen. However, this was accomplished after some effort and the incision in the abdominal wall was closed. The infant appeared to be in good condition immediately after completion of the operation, but in a short time the respirations became very rapid and the temperature rose to 107°, and the infant died about two hours later. An autopsy was not permitted. A complicating factor was present which may have played a part in this death. The operation was performed during a period of extremely high atmospheric temperature, 110° F. on the day of operation. Because of the poor condition of the infant it was not thought advisable to further delay the operation.

#### SUMMARY

Most cases of congenital diaphragmatic hernia showing disturbances in infancy do not live beyond the first year of life. For this reason, there must be early recognition and prompt surgical intervention, even in the first few hours, if successful treatment is to be accomplished.

A difficulty which is often encountered in the surgical repair is the closure of very large defects in the diaphragm. This may be overcome by making use of the renal fascia which is ideally suited for this purpose. A technique which involves the use of this fascia is described here.

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would then be apparent that the liver was damaged. This assumption cannot be made, and experimental evidence attests the fact that in order for the blood to show a hyperbilirubinemia, indicating impairment of the function of the liver, a moderately advanced and generalized parenchymal damage must be present. The test was used accepting 1.0 mg. to 3.0 mg. per liter as a normal range of bilirubin values.

The bromsulphalein dye test has proved its merit as a test of liver function, although the same objection may be raised as in the use of blood bilirubin determinations; that is, the liver damage must be extensive before a retention of the dye will occur. This did not contraindicate its use in the series of cases in this study where the test was carried out on the day before operation establishing an estimate of the hepatic function. The dye test was carried out on the first postoperative day and then every other day until the retention was the same or less than the preoperative level. Thus, all patients were followed over an extended period of time and it was possible to gain an insight into the liver damage produced. Soffer<sup>6</sup> stated: "In any particular case that is followed over an extended period of time with an individual test, the results will indicate whether the hepatic lesion is becoming more extensive or is regressing." Five milligrams of the dye per kilogram of body weight were used throughout the series of tests and the blood specimens were collected 30 minutes after the dye administration. A dye retention of 10 per cent or less was considered to lie within normal limits; however, if a preoperative retention of dye was 5 per cent and the first postoperative day retention was 10 per cent, the liver was considered to have been damaged.

In a selection of the cases for this study an attempt was made to avoid those in which suspected hepatic damage existed; however, in a few instances patients were selected who were considered to have had liver damage preoperatively. Excluding Case 13 (long-standing chronic cholecystitis with cholelithiasis)<sup>12</sup> and Cases 16, 17, and 79 (3 patients with pulmonary tuberculosis),<sup>13</sup> the remaining cases of 100 were considered to have had a normal hepatic function. No attempt was made to exclude cases with acute infections, such as appendicitis, pyogenic abscess, and osteomyelitis, for liver damage could not be assumed to be present. With the few exceptions, the patients were not selected, and the observations were made on the patients as they were admitted to the surgical service.

In reviewing the literature regarding the effects of anesthesia on liver function, it was learned that most of the experimental efforts had been carried out in animals; however, these results have been accurate and conclusive in guiding us in a selection of a suitable anesthetic for a given patient. In 1909, Whipple and Sperry<sup>14</sup> observed that two hours of chloroform anesthesia resulted in hepatic damage which required two

vention damage the liver? If so, the damage produced occurs simultaneously with the damage produced by the anesthetic, and this factor cannot be eliminated. Second, does the measurement of one function of the liver give a true conception of the damage produced by an anesthetic? The functions of the liver are so numerous that one test cannot pretend to portray the true status of liver function; however, numerous tests relating to specific functions, if properly correlated, will give a fair estimate of the efficiency of the liver. In determining the damage produced by anesthetics, however, all these tests would not be used, for as Soffer<sup>6</sup> has stated: "In testing multiple functions of the liver one positive test is as significant an index of the presence of hepatic damage as would be the case if all the tests were abnormal." Third, if one finds himself in a dilemma regarding which of the various liver functions to measure, he is as equally confused as to which of the numerous tests to select in determining this specific function.

In 1925, Greene, Walters, Snell, Rowntree, and McVicar<sup>9</sup> reviewed the various tests of hepatic function and were of the opinion that the most practical tests were the icterus index, the van den Bergh, and the bromsulphalein dye test. In 1928, Piersol and Rotham<sup>10</sup> considered bromsulphalein to be the most satisfactory dye test. In 1932, Robertson, Swalm, and Konzelmann<sup>11</sup> in a study of the various liver function tests concluded that the bromsulphalein dye test was the most sensitive test. Takane<sup>5</sup> in 1932, working with experimentally produced liver damage, found the bilirubin excretory test (bilirubin injected intravenously) superior to the Congo red excretory test in determining hepatic function. Teneff<sup>7</sup> in 1935 carried out a group of tests on each of a series of patients, and in his experience offered the following tests as the most desirable: glycemic curve after the oral administration of glucose, bengal red dye test, blood bilirubin, and daily urobilin excretion. Soffer<sup>6</sup> in 1935 discussed thoroughly the particular value and indications for each test and offered comparative data indicating that the bilirubin excretory test was the most sensitive of the commonly used tests in determining the excretory function of the liver. The bromsulphalein dye excretory test was the second most sensitive. At the present time, it is apparent that the van den Bergh test, icterus index, and galactose tolerance test are selected for the jaundiced patients by the majority of clinicians, while the bilirubin and bromsulphalein dye excretory tests are selected for the nonjaundiced patients with probable hepatic damage.

Throughout the series of 100 cases to be presented, the bromsulphalein excretory dye test was used, and in the first 18 cases blood bilirubin determinations were obtained at the same time the dye tests were performed. If it could be assumed that no increase in hemolysis of red blood cells takes place during an operation under anesthesia, and an abnormal amount of bilirubin appear in the blood postoperatively, it

would then be apparent that the liver was damaged. This assumption cannot be made, and experimental evidence attests the fact that in order for the blood to show a hyperbilirubinemia, indicating impairment of the function of the liver, a moderately advanced and generalized parenchymal damage must be present. The test was used accepting 1.0 mg. to 3.0 mg. per liter as a normal range of bilirubin values.

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to three weeks for recovery. In 1922, LaRocque<sup>16</sup> in a clinical study of the effect of anesthesia on hepatic function arrived at the following conclusions: (1) chloroform always produces liver damage; (2) ether produces liver damage which may be as severe and prolonged as with chloroform, but which differs in that the damage with ether is not as constant as with chloroform; (3) nitrous oxide is the only anesthetic which does not injure the hepatic cells; and (4) nitrous oxide and ether combined reduce considerably the chance of liver damage as compared to ether alone. Sanford, Rosenthal and Bourne<sup>15</sup> in 1928 confirmed the work of Whipple and Sperry and considered chloroform anesthesia to be synonymous with chloroform poisoning. One-half hour of chloroform anesthesia resulted in a hyperbilirubinemia for three days and an abnormal retention of bromsulphalein dye for eight days. Two hours of chloroform anesthesia resulted in a hyperbilirubinemia for eight days and an abnormal dye retention for six weeks. These authors were unable to find definite liver pathology after using ether; however, there was a transient retention of bromsulphalein dye, the degree of hepatic damage paralleling the duration of ether anesthesia. In using nitrous oxide and ethylene with the exclusion of cyanosis, there was no evidence of hepatic damage. With nitrous oxide and ethylene in a closed chamber with poor oxygenation, there was both an immediate and a prolonged abnormal dye retention. Sanford and others concluded that "cyanosis in itself increased the toxicity of an anesthetic on the liver." In 1931, Bourne, Bruger, and Dreyer<sup>17</sup> studied the action of avertin on man and dogs. They came to the conclusion that avertin compared favorably with the inhalation anesthetics relative to its effect on hepatic function. In the human cases there was no abnormal retention of bromsulphalein dye twenty-four hours after avertin anesthesia. In using ether, hepatic function was found to be slightly depressed for twenty-four hours with a return to normal in forty-eight hours. In 1931, Bourne and Raginsky<sup>18</sup> showed that repeated administration of avertin to dogs produced only minimal hepatic damage. In dogs with liver damage previously produced by chloroform, avertin was found to produce a 5 to 30 per cent additional damage. This additional damage disappeared in from twenty-four to forty-eight hours and in no manner affected the total recovery period from chloroform. Takane<sup>8</sup> in 1932, experimenting with rabbits, showed that chloroform produced marked hepatic damage; avertin produced definite liver damage for two days; and nitrous oxide, oxygen, and ether combined were harmless with only a transient retention.

Of the 100 cases receiving an anesthetic for surgery, 49 received nitrous oxide, oxygen, and ether vapor; 27 received nitrous oxide and oxygen; 13, avertin; 8, intraspinal procaine and pantocaine with occasional supplementary nitrous oxide; 2, local infiltration with pro-

caine; and 1, open ether. No attempt was made to include an equal number of patients under each type of anesthesia used; however, these six different anesthetics comprise the types used either individually or in combination as a balanced anesthesia.

Blood bilirubin determinations were carried out preoperatively and postoperatively on the first 18 cases along with the bromsulphalein dye retention test. There was an abnormal bilirubinemia in several instances, but the dye test was so much more sensitive that it was not considered worth while to continue with the blood bilirubin determinations.

Fifty-one per cent of all the patients receiving nitrous oxide, oxygen, and ether vapor showed impaired liver function the first postoperative

TABLE I

THE EFFECT OF ANESTHESIA ON LIVER FUNCTION. ONE HUNDRED SURGICAL CASES STUDIED—GENERAL CONSIDERATION

TYPE OF ANESTHESIA	TOTAL NUMBER OF CASES	NUMBER AND PER CENT SHOWING DYE RETENTION†	AVERAGE DURATION* OF ANESTHESIA	AVERAGE AGE	AVERAGE AGE WITH DYE RETENTION	AVERAGE AGE WITHOUT DYE RETENTION
N <sub>2</sub> O and O <sub>2</sub> and ether vapor	49	25 51%	Longest, 210 min. 122 min. Shortest, 40 min.	Oldest 72 33.2 yr. Youngest 12	39.1 yr.	27.3 yr.
N <sub>2</sub> O and O <sub>2</sub>	27	9 33½%	Longest, 180 min. 80 min. Shortest, 30 min.	Oldest 75 40 yr. Youngest 16	52.2 yr.	33.9 yr.
Avertin	13	10 77%	Longest, 210 min. 137 min. Shortest, 60 min.	Oldest 58 34 yr. Youngest 15	39.0 yr.	19.0 yr.
Spinal	8	4 50%	Longest, 150 min. 99 min. Shortest, 40 min.	Oldest 67 48 yr. Youngest 20	42.0 yr.	54.0 yr.
Local (procaine)	2	0	Longest, 40 min. 40 min. Shortest, 40 min.	Oldest 34 29.5 yr. Youngest 25	0	29.5 yr.
Open (ether)	1	1-100%	90 min.	36 yr.	36.0 yr.	0

\*This is the time expressed in minutes with respect to operating time and does not include the time of postoperative narcosis or time during which the anesthetic is exerting its influence after operation.

†In using the expression Dye Retention, it is used synonymously with liver damage.

day with a rapid decline in the percentage showing liver damage at the end of forty-eight hours; however, on the third postoperative day 18 per cent showed a persistent abnormal retention of the dye. By the thirteenth postoperative day the hepatic function in all the cases had returned to the preoperative level. Thirty-three and three-tenths per cent of the patients receiving nitrous oxide and oxygen showed hepatic damage on the first postoperative day with a gradual return to the preoperative level of dye retention by the eleventh postoperative day. Seventy-seven per cent of the patients receiving avertin showed evidence of liver damage on the first postoperative day with an evident prolonged return to the preoperative level of hepatic function in the majority of



cases; however, by the thirteenth day after operation the liver had entirely recuperated from the damage. Fifty per cent of the patients receiving spinal anesthesia revealed evidence of liver damage on the first postoperative day with a rapid recovery from the liver damage by the seventh day. There was no abnormal retention of the dye above the pre-operative level in the two cases receiving local anesthesia. In the single case receiving open ether, liver damage resulted with recovery by the fifth postoperative day (Tables I and II).

TABLE II

THE EFFECT OF ANESTHESIA ON HEPATIC FUNCTION RELATIVE TO THE NUMBER OF DAYS REQUIRED FOR THE LIVER TO RECUPERATE FROM THE DAMAGE PRODUCED

TYPE OF ANESTHESIA	NUMBER OF CASES	NUMBER AND PER CENT OF PATIENTS SHOWING DYE RETENTION ON VARIOUS P.O. DAYS FOLLOWING ANESTHESIA						
		I	III	V	VII	IX	XI	XIII
N <sub>2</sub> O and O <sub>2</sub> and ether vapor	49	25 51%	9 18%	5 10%	2 4%	2 4%	2 4%	0
N <sub>2</sub> O and O <sub>2</sub>	27	9 33½%	5 18%	3 11%	1 4%	1 4%	0	0
Avertin	13	10 77%	5 39%	3 23%	2 16%	1 8%	1 8%	0
Spinal	8	4 50%	3 37%	1 12%	0	0	0	0
Ether (open)	1	1 100%	1 100%	0	0	0	0	0
Local	2	0	0	0	0	0	0	0

The duration of anesthesia plays a significant rôle in the hepatic damage produced by an anesthetic (Table III). If the duration of anesthesia does not exceed an hour, only a small percentage of the cases reveal evidence of hepatic damage. This is well illustrated in the cases receiving nitrous oxide, oxygen, and ether vapor, and in the cases receiving nitrous oxide and oxygen, for in these two groups the majority of the cases fall.

Age is an important factor in determining the effect that an anesthetic will have upon hepatic function, while sex does not appear to be a factor (Tables I and IV). The average age of patients showing hepatic damage with nitrous oxide and ether vapor anesthesia was twelve years more than the average age of those patients who did not reveal evidence of liver damage. The cases receiving nitrous oxide and oxygen differed as to the average age by twenty years. In using avertin the average ages differed by twenty years. In the cases receiving spinal anesthesia, the average age with abnormal retention of the dye was less than the average age without retention of the dye.

As previously mentioned, 4 cases were selected because it was considered that hepatic damage existed. In addition to these cases there were 20 other cases revealing unsuspected liver impairment prior to operation. It was an interesting side issue to determine how these livers

TABLE III  
LENGTH OF ANESTHESIA IN RELATION TO HEPATIC DAMAGE PRODUCED

TYPE OF ANESTHETIC	60" OR UNDER		61" TO 90"		91" TO 120"		121" TO 150"		151" TO 180"		181" AND OVER	
	NO. CASES	NO. WITH RE-TENTION	NO. CASES	NO. WITH RE-TENTION	NO. CASES	NO. WITH RE-TENTION	NO. CASES	NO. WITH RE-TENTION	NO. CASES	NO. WITH RE-TENTION	NO. CASES	NO. WITH RE-TENTION
N <sub>2</sub> O + O <sub>2</sub> and ether vapor	7	1 14%	16	6 38%	10	8 80%	4	2 50%	8	6 75%	4	2 50%
N <sub>2</sub> O + O <sub>2</sub>	12	1 9%	5	2 40%	7	5 71%	2	1 50%	1	1 100%	0	0
Avertin	2	1 50%	1	1 100%	2	2 100%	1	1 100%	6	4 66%	1	1 100%
Spinal	2	1 50%	2	2 100%	1	0	3	1 33%	0	0	0	0
Local	2	0	0	0	0	0	0	0	0	0	0	0
Open ether	0	0	1	1 100%	0	0	0	0	0	0	0	0

TABLE IV  
RELATIONSHIP OF AGE AND SEX IN DETERMINING THE EFFECT OF ANESTHESIA ON LIVER FUNCTION

TYPE OF ANESTHESIA	NUMBER OF MALES	NUMBER OF FEMALES	NUMBER OF MALES WITH RETENTION	NUMBER OF FEMALES WITH RETEN- TION	AVERAGE AGE OF MALES WITH RETEN- TION	AVERAGE AGE OF FEMALES WITH RETEN- TION	AVERAGE AGE OF MALES WITHOUT RE- TENTION	AVERAGE AGE OF FEMALES WITHOUT RE- TENTION
N <sub>2</sub> O and O <sub>2</sub> and ether va- por	31	18	17 56%	8 44%	40.5 yr.	36.2 yr.	27.9 yr.	26.6 yr.
N <sub>2</sub> O and O <sub>2</sub>	12	15	3 25%	6 40%	55.7 yr.	50.5 yr.	31.6 yr.	36.2 yr.
Avertin	7	6	7 100%	3 50%	46.0 yr.	28.0 yr.	22.0 yr.	17.5 yr.
Spinal	8	0	4 50%	0	42.0 yr.	0	54.0 yr.	0
Local	2	0	0	0	0	0	29.5 yr.	0
Ether (open)	0	1	0	1 100%	0	36.0 yr.	0	0

behaved (Table V). Additional liver damage was produced in 8 of the 9 cases receiving nitrous oxide, oxygen, and ether vapor inhalation anesthesia, and in all the cases receiving avertin. The majority of the cases receiving nitrous oxide and oxygen resulted in further impairment of liver function. This group compared favorably with the general group (Table I) as to age and more than favorably as to the duration of anesthesia. The cases showing preoperative impaired hepatic function recuperated from the additional liver damage produced by the anesthesia in an even and gradual decline to return to the preoperative level of abnormal dye retention by the eleventh postoperative day.

TABLE V

THE EFFECT OF ANESTHESIA ON HEPATIC FUNCTION WITH EVIDENCE OF IMPAIRED HEPATIC FUNCTION PRIOR TO THE ADMINISTRATION OF ANESTHESIA: RELATIVE TO AGE, DURATION OF ANESTHESIA, AND DAYS REQUIRED FOR LIVER FUNCTION TO RETURN TO ITS PREOPERATIVE STATUS

TYPE OF ANESTHESIA	NUMBER OF CASES WITH LIVER DAMAGE PRIOR TO ANESTHESIA	AVERAGE DURATION OF ANESTHESIA	AVERAGE AGE	NUMBER AND PER CENT OF PATIENTS SHOWING DYE RETENTION ABOVE PRE-OPERATIVE LEVEL ON VARIOUS POST-OPERATIVE DAYS						
				I	III	V	VII	IX	XI	XIII
N <sub>2</sub> O and O <sub>2</sub> and ether V	9	110 min.	47.2 yr.	8 89%	6 67%	4 44%	1 11%	1 11%	0	0
N <sub>2</sub> O and O <sub>2</sub>	11	90 min.	48.0 yr.	6 55%	3 27%	2 18%	0	0	0	0
Avertin	2	125 min.	36.5 yr.	2 100%	1 50%	0	0	0	0	0
Spinal	0	0	0	0	0	0	0	0	0	0
Local	2	40 min.	29.5 yr.	0	0	0	0	0	0	0
Ether (open)	0	0	0	0	0	0	0	0	0	0

In carrying out the postoperative dye tests, it soon became obvious that the majority of those patients who were enjoying a smooth and uneventful convalescence seldom revealed evidence of impaired liver function. On the contrary, if the patient was having marked nausea and vomiting, fever, generally knocked out and below par, his chances of showing an abnormal retention of dye could usually be predicted (Table VI). In 51 patients without abnormal dye retention postoperatively and who had a smooth and uneventful convalescence, 90 per cent were

TABLE VI

RELATIONSHIP OF DYE RETENTION TO POSTOPERATIVE COURSE

POSTOPERATIVE CASES WITH DYE RETENTION				POSTOPERATIVE CASES WITHOUT DYE RETENTION		
49 PATIENTS				51 PATIENTS		
SYMPTOMS	NO SYMPTOMS	HIGHER RETENTION AFTER 1ST POSTOPERATIVE DAY	DEVELOPED INFECTION	SYMPTOMS	NO SYMPTOMS	DEVELOPED INFECTION
27, or 55%	22, or 45%	5, or 10%	5, or 10%	5, or 10%	46, or 90%	1, or 2%

classified as being symptom free. In the 49 cases which showed impaired hepatic function by the anesthesia, 55 per cent were classified as having symptoms. No attempt will be made to explain whether the symptoms result from impaired function or vice versa; however, 5 of the cases with symptoms and abnormal dye retention revealed higher retention of the dye after the first postoperative day. This rise in dye retention, after the first postoperative day, is not in keeping with liver damage produced by anesthetics, and in these 5 cases at least, the increased damage must be attributed to the complications. One case had paralytic ileus, one a wound infection with a question of meningitis; one had marked abdominal distention with delirium, one had a severe wound infection, and the fifth case was generally below par without any definite cause for further liver damage after the first postoperative day.

This brings up the rôle of infection commonly encountered in surgical cases and the relation of infection to impairment of hepatic function, exclusive of diseases of the liver and biliary tract. Brochner and Mortensen<sup>19</sup> studied 50 cases with acute febrile diseases in 1934 and 13 cases showed abnormal retention of bilirubin in using the bilirubin excretory test. This test revealed marked impairment of liver function in chronic sepsis. In 4 cases of pneumonia, 1 of encephalitis, and 1 of tuberculous meningitis, hepatic damage was found to be present. Patients with active pulmonary tuberculosis<sup>13</sup> have been proved to have an associated liver damage. In this series of 100 cases the total number with demonstrable preoperative infection was 13. Of the 13, 5, or 39 per cent, revealed the presence of preoperative impaired hepatic function. Eighty-seven revealed no apparent infection, and of this group 19, or 21 per cent, had preoperative liver damage (Tables VI and VII). In the 49 patients with postoperative hepatic damage, 5, or 10 per cent, had accompanying infection. Three had wound infection, 1 a pneumonitis, and 1 an upper respiratory infection. In the 51 cases without liver damage, postoperatively, 1 had a wound infection, and the liver function remained normal as determined by the dye test. The cases without evidence of impaired liver function on the first postoperative day were not followed further, and this no doubt explains the greater frequency of infection in the cases with abnormal dye retention in that the latter cases were followed over a long period of time.

#### COMMENT

A series of 100 surgical cases was studied relative to the effect of anesthesia on hepatic function. The suspected cases of hepatic damage were excluded with the exception of 4 cases; however, 20 additional cases of unsuspected liver damage were found to be present in the preoperative series. The bromsulphalein dye excretory test was used throughout, accepting 10 per cent or less as a normal retention. Five milligrams of

TABLE VII  
CASES SHOWING INFECTION—RELATION OF LIVER FUNCTION PREOPERATIVELY AND POSTOPERATIVELY

CASES SHOWING IMPROVING TENDENCY									
CASE NO.	SEX	DIAGNOSIS	AGE	OPERATION	ANESTHESIA	DURATION OF ANESTHESIA	LIVER FUNCTION PREOPERATIVE	LIVER FUNCTION POSTOPERATIVE	REMARKS ON POST-OPERATIVE COURSE
13	F	Chronic cholecystitis; c. d. stone	58	Cholecystectomy, cholecystectomy	N <sub>2</sub> O and O <sub>2</sub> and local	120 min.	I 60% III 80% V 80% VII 40%	I and 2. Distention, nausea, and vomiting, thereafter O.K.	
15	M	Chronic empyema (rt.)	20	Schede T.P.	N <sub>2</sub> O and O <sub>2</sub>	60 min.	I 10% 10%	Uneventful	
16	F	Pulmonary thc. (left)	24	1st stage T.P.	N <sub>2</sub> O and O <sub>2</sub>	120 min.	I 30% 30%	Uneventful	
17	M	Pulmonary thc. (left)	25	4th stage T.P.	N <sub>2</sub> O and O <sub>2</sub>	75 min.	I 60% 60%	Uneventful	
28	M	Inadequately drained abscess mediastinum	25	I. and D. secondary	N <sub>2</sub> O and O <sub>2</sub>	40 min.	I 10% 10%	Uneventful	
31	F	Abscess forearm	48	I. and D.	N <sub>2</sub> O and O <sub>2</sub>	40 min.	I 5% 5%	Uneventful	
43	M	Chronic osteo rt. femur	21	Sauzerization	Spinal	75 min.	I 10% III 20% V 15% 10%	I. T 102°—anorexia. 3. Same. 5. T 99°, then O.K.	
51	M	Osteo foot	47	Sequestrectomy	N <sub>2</sub> O and O <sub>2</sub> and ether V.	35 min.	I 5% III 25% 5%	Uneventful	
59	M	Acute appendicitis	20	Appendectomy	N <sub>2</sub> O and O <sub>2</sub>	40 min.	I 5% 5%	Uneventful	
65	M	Tenocapsynovitis hand	34	I. and D.	Local	40 min.	I 15% 15%	Uneventful	
66	M	Acute appendicitis	19	Appendectomy	N <sub>2</sub> O and O <sub>2</sub>	60 min.	I 3% 3%	Uneventful	
82	M	Osteomyelitis of amp. stump	58	Sequestrectomy	Spinal	40 min.	I 5% 5%	Uneventful	
87	M	Subphrenic abscess	43	I. and D.	N <sub>2</sub> O and O <sub>2</sub>	85 min.	I 15% III 30% V 25% 15%	I and 3. Marked vomiting	

Total no. cases with preoperative liver damage, 24.

Total no. cases with preoperative infection, 13; 5, or 39%, liver damage.

Total no. cases without apparent preoperative infection, 87; 19, or 21%, liver damage.

the dye per kilogram of body weight were given the patient and a sample of blood was taken 30 minutes after injecting the dye intravenously. The test was carried out on the day preceding operation and on the first postoperative day. If there was an abnormal dye retention the first postoperative day, the test was repeated every other day until the dye retention was within normal limits or had returned to the level of preoperative retention.

Avertin produces hepatic damage in a higher percentage of cases and to a greater degree than nitrous oxide, oxygen, and ether vapor anesthesia; nitrous oxide and oxygen; spinal; local; and open ether. The liver is slower in recuperating from the damage produced by avertin than from the other four types of anesthesia which produced hepatic damage. Nitrous oxide and oxygen results in liver damage in a smaller percentage of the cases than nitrous oxide and ether vapor, and spinal anesthesia; however, the damaged liver from nitrous oxide and oxygen recuperates at about the same rate as the hepatic damage produced by spinal, and ether vapor with nitrous oxide. Local anesthesia did not produce liver damage; however, the other five types of anesthetics used produced hepatic damage in varying degrees: avertin is the most toxic to the liver, and in order of decreasing toxicity, nitrous oxide and ether vapor, spinal, nitrous oxide and oxygen, and local anesthesia may be listed.

The longer the anesthesia (avertin, inhalation anesthetics, or spinal), the greater the chance of liver damage.

Sex does not influence the effect of anesthesia on hepatic function. The older the patient the greater will be his chances of hepatic damage from an anesthetic.

If impaired liver function exists prior to the administration of avertin, or nitrous oxide, oxygen, and ether vapor anesthesia, it is a certainty that additional liver damage will result. In the majority of cases where impaired function of the liver exists, nitrous oxide and oxygen anesthesia will result in additional hepatic damage. The impaired liver recuperates from the additional damage due to anesthesia at about the same rate as the normal preoperative functioning liver recuperates from the damage by an anesthetic.

The maximum hepatic damage produced by the group of anesthetics used in this series occurred during the first twenty-four hours postoperatively.

Patients with uncomplicated and smooth convalescence seldom show hepatic damage. If a rise in the percentage of retention of the dye occurs after the first postoperative day, a complication will usually be found to be present.

Excluding infections of the liver and biliary tract, pulmonary tuberculosis, chronic sepsis, and overwhelming infections, surgical cases with

an associated infection such as acute appendicitis, abscesses, and wound infections, will not reveal evidence of impaired hepatic function resulting from the infection per se.

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# CHOICE OF ANESTHETIC AGENTS AND METHODS OF THEIR ADMINISTRATION FOR DIABETIC PATIENTS

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THE selection of the most suitable anesthetic for the patient for whom factors in addition to those arising from the nature of the surgical demands must be considered constitutes a problem worthy of the combined attention of surgeon, clinician, and anesthetist. This is especially true in cases in which the surgical condition is complicated by diabetes mellitus. This type of patient tolerates certain anesthetics well, others rather well, and still others badly. One might employ only those agents which the patient tolerates well, except for the fact that they do not, in all instances, meet the needs of the surgeon.

A consideration of the peculiar problems of the diabetic patient reveals that the greatest danger is acidosis, under the shadow of which he must live his whole life. Paramount in the prevention of this complication are proper diet and facilities for its combustion and adequate elimination. Insulin has afforded a remarkable reduction in the operative mortality among diabetic patients. This has been emphasized by Walters, Meyerding, Judd, and Wilder, who reported a mortality of 3.3 per cent in 2,086 cases in which operations were performed on diabetic patients.

Anesthetic agents, by the very quality which renders them capable of inducing anesthesia, interfere with the normal functioning of the cells which they affect. If the function of the cells of the liver, pancreas, and kidney of a diabetic patient is sufficiently disturbed, acidosis results. If the acidosis is not too severe or of too long duration, and if it is recognized, it can be combated successfully and no permanent damage will result. Thus, its complete prevention is not essential or indeed, in many cases, possible.

Chloroform and ether, when used to produce anesthesia, cause hyperglycemia.<sup>16, 21</sup> Foster said that the increase in the value for the blood sugar coincident with ether anesthesia is probably the result of defective utilization of carbohydrate. Rabinowitch said that ether prevents the conversion of dextrose into glycogen and the storage of the latter in the liver. It also interferes with the metabolism of the

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glycogen already there, and in these ways causes hyperglycemia. This interference, according to Simpson, is attributable, at least in part, to asphyxiation of tissues. Sansum and Woodyatt found that when ether is administered to phlorhizinized dogs, hyperglycemia results immediately. They explained this on the basis of the transformation of hepatic glycogen to sugar in the presence of asphyxia. Ether diminishes the excretion of urine, and therefore also diminishes the excretion of nitrogen, dextrose, and acetone bodies. Katsch and von Friedrich noted that ether stimulates the external secretion of the pancreas. Joslin and Simpson suggested that, in consequence of this action, it might also diminish the internal secretion of this gland.

Stehle and Bourne expressed the opinion that ether increases the hydrogen ion concentration of the blood and lowers the carbon dioxide combining power of the plasma. In experiments on dogs, van Slyke, Austin, and Cullen found that ether anesthesia always caused an increase in the hydrogen ion concentration in all cases, and an accompanying decrease in the alkaline reserve, which was the result of the introduction of acid into the blood or the withdrawal of base from it. Leake, Leake, and Koehler confirmed the work of van Slyke, Austin, and Cullen and observed that the acidosis which develops is not dependent on the respiratory activities, and therefore is not the result of acapnia. They indicated that the acidosis is more probably due to loss of base from the blood than it is to the addition of acid, as they found no marked increase in the concentration of acetone bodies in the blood during prolonged ether anesthesia. Cullen and his associates found that the larger part of the decrease in alkali reserve which occurs as a result of ether and chloroform anesthesia takes place early in the course of the anesthesia. The occurrence of this decrease together with the prompt increase in hydrogen ion concentration suggests an uncompensated acidosis. Gross said that the concentration of acetone bodies does not tend to increase as a result of anesthesia with ether or chloroform and he did not find any significant increase in the concentration of lactic acid in the blood under these conditions. Blum demonstrated that the hypodermic injection of beta-oxybutyric acid into normal dogs does not cause the appearance of diacetic acid and acetone in the urine, but if the dog is under chloroform anesthesia, a marked acetonuria results. It is a common thing to find acetone present in the urine of nondiabetic patients following ether anesthesia, but this probably is frequently accounted for by semistarvation from restricted intake of food (carbohydrate).

Hagen called attention to the striking similarity between the disturbances of metabolism associated with the acidosis of diabetes and that resulting from ether anesthesia. This similarity includes even the narcotic effects. He expressed the opinion that "a (diabetic) patient free from acidosis, with an ample supply of alkaline salts and water

in the body, a blood sugar within normal limits and in a normal state of nutrition may be considered as good an operative risk as a non-diabetic patient." Wilder agreed with this statement although he excepted those patients who had diabetes associated with arteriosclerosis and who were subjected to operations on the sigmoid colon. In such cases, the danger of leakage from delayed union of the intestine is always present as the blood supply is poor. Joslin emphasized the fact that administration of chloroform interfered with carbohydrate metabolism and that this interference disturbed the metabolism of fat and resulted in acidosis and coma. The concentration of fat in the blood is increased by ether anesthesia. Sansum and Woodyatt found acetonuria following etherization of normal dogs. Ether necessitates fasting before anesthesia and, by causing postanesthetic nausea and vomiting, interferes with the ingestion of food.

Most writers are agreed that ether and chloroform are dangerous anesthetics for diabetic patients.<sup>3, 5, 7, 9, 12, 26</sup> They condemn chloroform altogether and advise avoiding ether if possible, but they admit that it may be safe if used carefully and in small amounts. Fitz said that ether is well tolerated by many diabetic patients but not in those cases in which the diabetes is complicated by sepsis, and not unless a small amount is sufficient. Judd and his colleagues said that ether is the anesthetic of choice for many diabetic patients. They found that the mortality was no higher with ether than with other anesthetics. Ether is not ideal from a medical viewpoint, but, as it produces better anesthesia and relaxation than anesthetic gases alone, it permits a more rapid operation and lessens shock. Lemann did not find any evidence of acidosis in several cases in which ether was administered to diabetic patients. Walters, Meyerding, Judd, and Wilder reiterated the opinion that ether is preferable if it shortens the duration of the operation. The importance of using as little ether and for as short a time as possible is realized by all who recommend its use.<sup>2, 35</sup> According to Fitz, the amount of ether used for 100 abdominal operations at the Mayo Clinic was only 46 per cent of the amount used in a similar series of cases in the average hospital elsewhere.

Mixtures of nitrogen and oxygen cause as much acidosis as nitrous oxide and oxygen. The acidosis is therefore the result of anoxemia. Acetylene acts much as nitrous oxide, but it is more effective and may therefore be used with larger amounts of oxygen and with a correspondingly lessened danger of acidosis.<sup>33</sup> Ethylene behaves as acetylene in this respect. Leake and Hertzman said that if sufficient oxygen to keep the oxygen saturation of the blood within normal limits is used with ethylene (92 per cent or more), no change in the chemical composition of the blood should be expected. These authors found that if there is no anoxemia when ethylene and oxygen are used to anesthetize dogs there is a slight fall in the hydrogen ion concentration

and carbon dioxide content of arterial blood but not beyond normal limits when anesthesia is maintained for half an hour. If anoxemia is present, however, there is an initial increase in arterial hydrogen ion concentration with inconstant changes in carbon dioxide content of the blood. This condition, which persists fifteen to twenty minutes, is followed by a fall in the hydrogen ion concentration and in the carbon dioxide content. It is impossible to maintain nitrous oxide anesthesia without anoxemia, but neither nitrous oxide nor ethylene influences the reaction of the blood so markedly or so rapidly as ether or chloroform.

Local anesthesia is recognized by many as one of the most favorable types of anesthesia for diabetic patients. Especially is this true of block anesthesia, for its use does not injure the operative site itself. It is inadvisable to employ procaine by local infiltration in a region which has a deficient circulation, on account of the danger of producing gangrene or infection.<sup>22, 23</sup> Dewes contended that the slight hyperglycemia which follows the use of local anesthesia (for extra-peritoneal operations) is due to the anesthetic agent. He said that the hyperglycemia is much greater in cases in which laparotomies are performed than it is in cases in which other operations are performed; in the former cases the value for the blood sugar sometimes is two to four times the normal figure. Lynn noted that the increase in the value for the blood sugar was 30 to 60 mg. per 100 c.c. following block anesthesia; this probably was attributable, at least in part, to a fall (about ten points) in the blood pressure.

Spinal anesthesia is generally conceded to be very useful for diabetic patients. Hailes contended, and with justification, that it should not be used in cases in which the patients were debilitated as such patients cannot tolerate a decrease in blood pressure, but diabetes itself is no contraindication to the use of spinal anesthesia. Vogel reported excellent results from the use of spinal anesthesia for amputation of the lower extremities of diabetic patients.

Preoperative and postoperative care of the diabetic patient is of great importance. Eliason recommended determination of blood sugar and carbon dioxide combining power of the plasma before operation. If the value for the carbon dioxide combining power is found to be low, he said that operation should be postponed until the acidosis has been overcome, for although the patient might survive the operation he might succumb to postoperative acidosis. Eliason also favored routine determinations of the values for the blood sugar and the carbon dioxide combining power of the plasma within five hours after operation.

Joslin advised the use of a small dose of morphine in order to avoid too great a respiratory depression, and McKittrick and Pratt did not use any opiate before operation, as opiates cause hyperglycemia. Le-

mann recommended the use of an extra carbohydrate feeding with an appropriate dose of insulin six to eight hours before the operation, and 20 c.c. of 50 per cent solution of dextrose with one or two units of insulin per gram of dextrose during the administration of the anesthetic. Intravenous administration of dextrose and insulin has not been used during operations at the clinic.

Chloroform is an especially dangerous anesthetic for diabetic patients and should not be used. Administration of ether to diabetic patients causes hyperglycemia, a concentration of blood fats, a suppression of renal function, and a pronounced tendency to acidosis. In spite of these obvious disadvantages it may be administered when its use shortens the operating time and facilitates the work of the surgeon, provided that the amount used is small.

Nitrous oxide and ethylene have only a slight tendency to cause acidosis and are satisfactory anesthetic agents for diabetic patients. It is essential that anoxemia be avoided. Procaine used as a local anesthetic is very valuable, especially when employed for block anesthesia. Local infiltration should be avoided in regions which are infected or which have an impaired circulation. Spinal anesthesia is useful for many operations on diabetic patients and has no contraindication peculiar to the disease.

Two hundred forty-four cases in which diabetic patients were operated on at the clinic from January 1, 1932, to January 1, 1934, were studied.<sup>29</sup> Of these patients, 108 were males and 136 were females. The youngest was six years of age and the oldest was eighty-two years.

Diabetes was graded on the basis of the severity of the disease;<sup>1</sup> thus, grade 1 includes those cases in which simple dietary regulation suffices to control the disease; grade 2 includes cases in which insulin is not required but strict and accurate regulation of the diet is necessary; grade 3 includes those cases in which the patients required 30 units or less of insulin and tolerated between 70 and 140 gm. of carbohydrates; grade 4 includes those cases in which more than 30 units of insulin are required in addition to a careful regulation of the diet.

Two hundred seventy-nine operations were performed on the 244 patients in this series. Tables were compiled to show the incidence of various complications and death in diabetes following anesthesia. In Table I the different anesthetic agents are listed with the number of times each was used in this series. Table II shows the ages of the patients and Table III shows the cases grouped according to the site of operation.

#### SUMMARY AND CONCLUSIONS

Among the complications three groups are of interest. In 5 cases the grade of the diabetes was increased, as shown by the need for additional insulin. In 2 of these cases this change was permanent, while in the third case it was only a temporary aggravation. In 9 cases infection

TABLE I  
MORTALITY AND INCIDENCE OF COMPLICATIONS FOLLOWING THE ADMINISTRATION OF VARIOUS ANESTHETICS IN OPERATIONS ON DIABETIC PATIENTS

ANESTHETIC	ANES- THE- SIAS	INCREASE IN SEVERITY OF DIABETES			COMPLICATIONS												DEATHS					
		NUM- BER	PER CENT	PER CENT	RESPIRATORY			CIRCULATORY			GENITO- URINARY			INFECTIONS					MISCEL- LANEOUS			
					NUM- BER	PER CENT	PER CENT	NUM- BER	PER CENT	PER CENT	NUM- BER	PER CENT	PER CENT	NUM- BER	PER CENT	PER CENT	NUM- BER	PER CENT	PER CENT	NUM- BER	PER CENT	PER CENT
Ether (1 to 4 oz.) with or without other agents	48	1	2.1		1	2.1						2	4.2		1	2.1				4	8.3	
Ether (4 to 8 oz.) with or without other agents	24				2	8.3		2	8.3										1	4.2	1	4.2
Ether with or without other agents, including less than 1 oz. of ether	76	3	3.9		2	2.6		1	1.3						1	1.3			3	3.9	7	9.2
Local or regional anesthetics used alone	33				1	3.0									1	3.0			1	3.0	2	6.1
Spinal anesthetic with or without gas	56	1	1.8		3	5.3		2	3.6			2	3.6		3	5.3			3		1	1.8
Cocaine	19											1	5.3									
Tribromethanol (avertin)	1																		1	100.0		



TABLE III  
MORTALITY AND INCIDENCE OF COMPLICATIONS ACCORDING TO SITE OF OPERATION

SITE OF OPERATION		COMPLICATIONS																		DEATHS	
		INCREASE IN SEVERITY OF DIABETES			RESPIRATORY			CIRCULATORY			GENITO-URINARY			INFECTIONS		MISCEL- LANEOUS					
OPERA- TIONS	NUM- BER	PER CENT	NUM- BER	PER CENT	NUM- BER	PER CENT	NUM- BER	PER CENT	NUM- BER	PER CENT	NUM- BER	PER CENT	NUM- BER	PER CENT	NUM- BER	PER CENT	NUM- BER	PER CENT			
Lower extremities <sup>4</sup> Perineum (including punch operation)* Abdomen Thorax and breast Upper extremities <sup>4</sup> Neck Head	16						1	6.3									3	18.8			
	58	1	1.2		6	7.2	1	1.7		2	3.4		1	1.7			1	1.7			
	83	2	15.4							2	2.4		3	3.6		3	3.6	5	6.0		
	13						1	7.7									1	7.7			
	8																1	12.5			
	58	2	3.4		3	5.5	1	1.7		1	2.3		1	1.7		1	1.7	4	6.9		
	43						1	2.3					1	2.3		2	4.6				

\*Transurethral prostatic resection.



TABLE II  
MORTALITY AND INCIDENCE OF COMPLICATIONS ACCORDING TO AGE OF PATIENTS

[illegible]

that statistics obtained on a larger group of cases will bear this out. Studies of other series may reveal that our conclusions may be explained by inclusion, in this group, of cases of infected diabetic gangrene or of the other cases of diabetes complicated by infection, in which such operations as emergency procedures are performed.

It is recognized, however, that infection and gangrene are not infrequently an intimate part of the syndrome of diabetes and therefore we feel that our conclusions are not unwarranted.

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followed the operation. Three of these cases are included under the heading "Genitourinary Complications" in the table. In 2 other cases there was delayed healing. In these last 2 cases the complications included conditions which often are encountered in cases of diabetes and which should not be attributed to the anesthesia except as the latter may have caused a transitory increase in the severity of the diabetes. The other complications encountered are those seen on any surgical service.

Of the 15 deaths in this series, the earliest occurred on the third postoperative day and the others occurred at longer intervals up to twenty-two days. It is difficult to blame an anesthetic for a death that occurs many days after the use of the anesthetic. It is interesting that in many of the postoperative notes in this group of cases mention was made of the fact that the diabetes was under reasonably good control. Nearly all the anesthetics in common use were employed in one or more of these fatal cases, but cyclopropane, tribromethanol (avertin), or cocaine were not used. The largest quantity of ether used was 7 ounces (210 c.c.), the next largest amount was 2 ounces (60 c.c.), and 1 ounce (30 c.c.) or less was used in the other cases; therefore, ether did not play a conspicuous part in a large percentage of these fatalities. The duration of operation and anesthesia in this group of cases averaged about sixty-three minutes, which is at least suggestive.

From these data we may be justified in concluding that the usual anesthetic agents may be used for a diabetic patient provided the diabetes is carefully controlled preoperatively and postoperatively. This is true provided that reasonable care is taken to avoid surgical procedures which are of unusually long duration and provided that the anesthetic is administered with reasonable skill, without the use of excessive amounts of ether. In Table I it may be noted that the mortality was least following the use of spinal anesthesia. Table II demonstrates that the danger of a fatal outcome following operation increases in direct proportion to the age of the patient. Thus, the mortality encountered in cases in which patients were below the fifth decade of life (44 patients) was 0; in the fifth decade it was 4.9 per cent, and in the seventh decade it was 10.1 per cent. In Table III one may be surprised to note that the mortality was highest for patients who underwent surgical procedures on the lower extremities. This, however, is readily explained. In the majority of these instances amputation was done for diabetic gangrene and infection. The risk was recognized, but it was deemed essential that the operation be undertaken. It appears that the risk of operation is greater for patients suffering from diabetes than it is for the average individual and that the danger encountered following surgical procedures varies directly with the grade of diabetes. We are not convinced, however,

## ACUTE APPENDICITIS

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THIS paper is a critical review and examination of 1,325 consecutive operations on acutely inflamed appendices performed at Mt. Sinai Hospital, Cleveland, from January, 1924, to November, 1935. We wish to emphasize the point that they were all acutely inflamed as reported by the pathologist and no case diagnosed as catarrhal or subacute has been included. The patients were operated on by the visiting staff and by the courtesy staff and include both private and ward service cases.

There were 748 males and 577 females. Seven hundred and eleven cases were between the ages of ten and thirty years.

TABLE I

AGE	MALE	FEMALE	TOTAL
Under 5 yr.	18	7	25
5 to 9 yr.	73	58	131
10 to 19 yr.	205	183	388
20 to 29 yr.	180	143	323
30 to 39 yr.	149	85	234
40 to 49 yr.	74	37	111
50 to 59 yr.	26	34	60
Over 60 yr.	14	16	30
Over 70 yr.	6	1	7
Age unstated	3	13	16
	748	577	1,325

The high percentage of patients operated on within 24 hours of the onset of symptoms was a factor in the low mortality rate. There were 1,020 cases admitted within 48 hours after onset, and of these 738 came within 24 hours. The duration of symptoms varied from 6 hours to 1 month. Those patients who had symptoms less than 12 hours totaled 226; 1 day, 512; 2 days, 282; 3 days, 122; 4 days, 46; 5 days, 20; 6 days, 13; 7 days, 29; 8 days to 1 month, 35. Although many of these cases were operated on early; many already had ruptured appendices with peritonitis. It is apparent that quite some degree of inflammation must be present in the appendix hours before it begins to give symptoms. Therefore, keen diagnostic ability and cooperation of the internist and family physician make possible early surgical intervention in acute appendicitis.

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whereas, the surgeon could and should have noted how severe the reactions were elsewhere. The report of localized peritonitis is only an index of what undoubtedly was more widespread and shows that the infection and reaction were no longer confined within the walls of the appendix. The mortality in this group was 5 per cent. For the whole series there were 57 deaths, or 4.3 per cent, and among these 57 deaths there were 7 cases in which the appendix was not removed or seen. There were 187 cases of ruptured appendices, 14.1 per cent of the series. Twenty-one of these died, a mortality of 11.2 per cent for ruptured appendicitis.

DeCourey reports the mortality rates for ruptured appendicitis from the Good Samaritan Hospital yearly from 1931 to 1935 varied from 24.5 per cent to 11.4 per cent, although he states that in a series of 50 cases he has reduced the mortality of ruptured appendicitis to 4 per cent by inserting a tube in the cecum after removing the appendix. He believes that decompression of the bowel is a very important factor in saving life in the case of ruptured appendicitis and his figures show that it should be given serious consideration. However, as again stated under the question of drainage, in our series 77 of the ruptured appendicitis cases were closed without drainage with a mortality of 4 cases, or 5.3 per cent; whereas, the mortality in the 110 cases of ruptured appendices that were drained was 15.4 per cent.

We found that a fecalith played an important rôle in the mortality figures. It was present in 184 appendices, or 14 per cent of the series, and was also in evidence in 18 of the 50 fatal cases, or 36 per cent of the total deaths. In other words, the 184 appendectomies where a fecalith was noted had a mortality of 9.8 per cent; whereas, the rest of the 1,141 appendectomies free from fecaliths carried a mortality of only 39, or 3.4 per cent. Thus the mortality in the presence of a fecalith was 3 times as high as in the absence of a fecalith. It was noted in all age groups, the youngest being three years of age and the oldest over sixty years. It appeared in 117 males and 67 females. They were operated on just as early as those cases in the general group. Seventy-eight (42 per cent) of these patients were admitted with symptoms of 1 day's duration; 58 (31 per cent), 2 days' duration. These percentages are almost the same as in the general group so that delay and age were not factors in the mortality figures.

In considering the pathologic conditions present in this group, we are struck with the severity of the disease process as reported by the pathologic laboratories. There were only 15 cases in this group admitted within 12 hours of the onset, as against 226 in the general group—a relative percentage of 8.1 per cent as against 17 per cent—yet 12 of these 15 early cases showed regional fibrinopurulent peritonitis. There was a total of 138 cases of this group of 184 which had regional fibrinopurulent peritonitis. Thus we can say that the infection spread more rapidly

Pain was the predominating symptom. It occurred alone in 248 cases; with nausea in 198; with vomiting in 408; with nausea and vomiting in 460.

In addition to the above cardinal symptoms the following were noted:

TABLE II

Chills	59
Diarrhea	28
Constipation	15
Dysuria	15
Urinary frequency	4
Backache	9
Sore throat	9
Nasopharyngitis	13
Fainting	2
Cold sweats	2
Malaise	5
Auricular fibrillation	1
Headache	24
Cases unstated	11

The white blood count, although not all important, should not be overlooked. It ranged from a low of 2,300 to a high of 46,000 in our series. If one considers a leucocytosis as beginning with 10,000, then a count is of little value as a diagnostic aid in 12 per cent of the cases. This is sufficient evidence to prove that the clinical history and physical findings are much more important and valuable in arriving at a diagnosis. We are all too familiar with the number of cases of gangrenous appendicitis with a low white blood count to permit the latter to deter us from operation. On the other hand, a very high white blood count with minimal physical findings may be accepted as an aid to diagnosis and an additional indication for operation.

TABLE III

W.B.C.	NO.
Below 5,000	4
5,000 to 7,900	37
8,000 to 9,900	104
10,000 to 11,900	126
12,000 to 14,900	319
15,000 to 19,900	376
20,000 to 24,900	148
25,000 to 29,000	39
Over 30,000	25

The cases with free purulent fluid or fibrin localized to the appendix bore a pathologic report of localized peritonitis and numbered 870. This report of the pathologist must not be taken too literally in considering the severity of these cases. In other words, it does not mean that there was no fibrin or peritonitis in the rest of the abdominal cavity. On the contrary, it means there probably was peritonitis elsewhere and more widespread, but the pathologist had only the appendix to examine;

hours in a six-year-old girl and yet a walled-off abscess was found at operation. Sometimes drains were inserted when there was no walled-off abscess. They were all cases, however, in which the surgeon found pus and in which he thought it was better not to look for the appendix or to attempt to remove it. This group of cases is highly instructive and is worth while analyzing more in detail. There were 16 females and 15 males. The youngest was a sixteen-month-old boy. The oldest, a female, definitely well over sixty years of age. Interesting enough, there were 16 cases under fifteen years of age, among whom there were only 2 deaths.

TABLE IV

DURATION OF SYMPTOMS	NO.
12 hr.	1
2 days	2
3 days	4
4 days	3
5 days	2
6 days	3
7 days	3
9 days	2
10 days	5
12 days	1
14 days	2
3 wk.	1
Unstated	2

By far, the greater number of cases were of more than 4 days' duration. There were 744 hospital days for 31 cases, for an average of 24 days per case. There were 26 abscesses; the rest had general peritonitis. Fourteen were drained properly by opening into the abscess and not penetrating the general abdominal cavity.

The six deaths in this group are interesting to analyze in detail:

CASE 1.—(N 2215) A white boy, aged eleven years, who had been ill six days before admission to hospital. An appendiceal abscess was drained through the rectum. The boy developed intestinal obstruction and peritonitis. An ileostomy was done, then an incision and drainage for abscess of the left side of the abdomen. He was given blood transfusions but nevertheless died on the forty-ninth hospital day. In retrospect, there is nothing that could have been done to save this boy except perhaps an earlier visit to the doctor.

CASE 2.—(N 230) A white woman, aged forty-six years, who had been ill ten days. She was explored for gallbladder disease. An appendiceal abscess was found which was inadvertently ruptured with a spill of pus into the general abdominal cavity. Peritonitis developed. The patient died in five days.

CASE 3.—(108-1225) A white male, aged forty years, who was ill three days. The patient had a diffuse peritonitis. He was also a diabetic. No attempt was made to locate the appendix. He had a massive intestinal hemorrhage on the eighth day, which at autopsy was found to have come from a gastric ulcer.

CASE 4.—(108-201) A nine-year-old girl, ill two days. The doctor decided upon a waiting policy. She was operated upon on the ninth day when her temperature, which had been coming down, suddenly began to rise. An appendiceal abscess was



beyond the walls of the appendix. There were 41 ruptured appendices in the 184 cases with fecaliths—22.3 per cent, as against 146 ruptured appendices in 1,141 cases—12.7 per cent. It is possible that the fecalith is responsible for a more rapid progress of the disease by tending to promote earlier rupture or earlier gangrene because of obstruction and resulting distention; consequently it is directly responsible for a great many deaths. Since this was written, Wangenstein and Bowers have published their results of experiments with obstructed appendices. Their results seem to agree with our clinical observations in this series of fecaliths.

Wilkie has pointed out that there are two primary and fundamental processes occurring in appendicitis. One is the acute infection of the wall of the appendix, the other an acute obstruction of the lumen of the appendix comparable to any other obstruction of the bowel. Kline stresses infection in false, microscopic diverticulae. Wilkie states in this type the rise of temperature is natural and inevitable. But in the obstructive type, this rise is absent during the early phase, at the very time when diagnosis is all important. While Wilkie does not believe that obstruction precedes infection in all cases, he does believe that blocking of the lumen, with consequent tension, is the real danger in appendicitis. It is unfortunate that the fecalith does not produce earlier symptomatology. In other words, this further brings out the fact well noted by many writers that symptoms and physical findings may be disproportionate to the pathologic condition present in acute appendicitis.

We examined our figures to note carefully the effects of drainage on mortality, morbidity, and complications. We have a sole positive indication for drainage, the localized walled-off abscess. It has been well established that a drain in the abdomen does not drain the abdomen for long, but that it becomes walled off in 14 to 20 hours or less and thereafter acts as a plug and a foreign body, thereby taxing the body economy. Nevertheless, a good many surgeons still drain the abdomen on the slightest provocation—so great is habit and the effect of past tradition. We consider first the 187 ruptured appendices with 21 deaths. Of these 187 cases, 110 were drained intraabdominally. Twenty-five were drained subfascially. There were 52 cases not drained at all, but these latter two groups may be added together totaling 77 cases in which the abdomen was actually not drained. There were 16 deaths in the group in which the abdomen was drained, a mortality rate of 16/110 or 14.5 per cent. There were 4 deaths in the group of cases with undrained abdomens, a mortality rate of 5.3 per cent. We believe these figures are important in emphasizing the dangers of drainage.

There were 31 cases operated upon in which drainage was the only procedure. There were 6 deaths (19.3 per cent). The average duration of symptoms was 7.9 days. The shortest duration of symptoms was 12

The following is a consideration of the complications:

1. Wound infection: We may consider every drained case a wound infection. There were 128 wound infections in the 794 nondrained cases, 16.18 per cent.

2. Pelvic abscess: Pelvic abscess is a common complication in appendicitis. There were 33 pelvic abscesses developed in the drained cases, 7 per cent. There were 11 pelvic abscesses in the subfascial drained group and 10 in the undrained group. These latter two groups may be added together for a total of 21 pelvic abscesses in 862 cases, 2.4 per cent. Therefore, pelvic abscess occurs over 3 times more frequently when the abdomen is drained.

Some attempt was made to correlate the amount of fluid present in the abdomen with the development of a pelvic abscess. Naturally this must be crude inasmuch as the actual amount of fluid present is never measured. Whether there is a large or small amount of fluid present is never measured. Whether there is a large or small amount of fluid noted on the chart differs with the temperament of the observer. Nevertheless, we thought it worth while to see what we could find.

TABLE V

	ABDOMEN NOT DRAINED	PELVIC ABSCESS FOLLOWED	SUB- FASCIAL DRAIN	PELVIC ABSCESS FOLLOWED	ABDOMEN DRAINED	PELVIC ABSCESS FOLLOWED
No free fluid	373		25		219	
Small amount free fluid	334	5	26	1	101	13
Large amount free fluid	76	5	16	10	61	20
Unstated	11		2		1	

We may group the cases where the abdomen was not drained and where it was subfascially drained together and we may also add the cases of no free fluid and the cases with a small amount of fluid together. Accordingly, we find that in the drained abdomens group where there was a large amount of fluid present, 20 out of 61, or nearly 30 per cent, developed a pelvic abscess. In the combined undrained groups, when there was a large amount of fluid present, only 15 out of 92 developed a pelvic abscess, 16.3 per cent. We may accordingly surmise that when there is a large amount of fluid present, a pelvic abscess may be a common complication regardless of whether the abdomen is drained or not, but nevertheless it is twice as frequent when the abdomen is drained. When there was a small amount of fluid present and the abdomen was drained, 13 out of 400, or 3.3 per cent, developed a pelvic abscess; but when the abdomen was not drained, only 6 out of 758, or 0.8 per cent, developed a pelvic abscess. Thus, drainage as a causative factor in the formation of a pelvic abscess is still more evident in this group of cases.

Fecal fistula occurred 16 times in the 462 drained cases—3.4 per cent. There was 1 fecal fistula in the subfascial drain group and 4 in the

opened through the free peritoneal cavity and was drained. She developed a fecal fistula and then a massive hemorrhage from the abdominal incision. She was transfused with whole blood several times. She died on the twenty-ninth day. This case does not militate against conservative treatment or against drainage only of an abscess. The case brings up the question of the proper method of draining an appendiceal abscess. It is always best if the abscess points toward the rectum or in the culdesac to drain through the rectum or vagina, respectively. However, when the abscess must be opened through the abdominal wall, great care must be taken to open the abscess laterally without opening the peritoneal cavity.

CASE 5.—(108-2784) A white male, sixty-eight years old, who had been ill three and one-half days, came into the hospital nearly moribund. At operation a large amount of free fluid was found and considerable pus. The appendix was retrocecal and gangrenous. No effort was made to remove it. The patient died in eight hours.

CASE 6.—(108-344). A fifty-nine-year-old woman, ill ten days. A diabetic in very poor condition. The patient had peritonitis plus a large abscess in the right iliac fossa which was ruptured accidentally, liberating a large quantity of very foul pus. The patient lived two days.

Thus, of the 6 deaths, 4 were apparently inevitable because of the patient's condition or the state of the disease on admission. Two patients might have been saved with different technique. The deaths in this group were due to peritonitis, intestinal obstruction, toxemia, massive hemorrhage (a) from abdominal wound, (b) from intestines—from gastric ulcer, paralytic ileus.

We next consider the effect of drainage on morbidity. There were 8,484 hospital days in the nondrained group. An average of 10.7 days. There were 69 cases in which a subfascial drain was used, but in which the abdominal cavity was not drained, that spent a total of 1,079 days in the hospital, for an average of 15.3 days. The closeness of this figure with that of 15.6 days in cases in which an abdominal drain was used would seem to indicate that the delayed healing of the abdominal wall was the only factor in prolonging their hospitalization.

The complications which arose in this group were general peritonitis, intestinal obstruction, decubitus ulcers, pelvic abscess, parotitis, submaxillary abscess, fecal fistula, massive hemorrhage from abdomen, massive intestinal hemorrhage, pleural effusion, subphrenic abscess, bronchial pneumonia, paralytic ileus, right lumbar abscess.

Of the 57 deaths, 38 patients were drained—approximately 65 per cent of the cases that died. Of course, it may be granted that these were mostly severe cases and included in these 38 deaths were 7 in which the appendix was not removed. There were 462 cases in which the abdomen was drained. The mortality rate for these is 8.03 per cent. In the nondrained group, the mortality is 2.21 per cent. Included in the series of 462 drainage cases are many cases which occurred in the earlier years of this study and doubtless would not be drained today.

48 hours, 62.3 per cent of the deaths. Four cases had had chills. There were 59 cases in our entire series who complained of chills. Chills, therefore, should not be looked upon as indicating a poor prognosis. Two cases had cough, 1 hiccoughs. Two cases were not operated upon. Six cases were operated upon and drained only. Thirty-seven cases were drained through the abdomen. One case was drained through the rectum. Fecalith was found and mentioned in 18 cases in which the appendix was removed. The 57 cases had a total of 599 hospital days, for an average 10.5 hospital days, but 18 of these cases lived but 2 days or less after admission which indicates a very virulent infection or that they were ill a long time and in poor condition and the operation hastened their end. Twenty-one cases, nearly 37 per cent, gave histories of having had cathartics and several more had had enemas.

Most writers find great difficulty in drawing the dividing line between the localized and the spreading types of peritonitis. We believe it is altogether too difficult and too hazardous to try to determine this at operation. Certainly if a McBurney incision is used, the view of the abdomen is quite limited. Most surgeons use this type of incision. The important factors in any infection are the virulence or numbers of the infecting organisms and the resistance of the patient. It seems to us that more and better information is given if the presence or absence of pus or cloudy fluid and the amount present are stated rather than to attempt to guess what type of peritonitis it is. Accordingly, we find in this group of 57 deaths that 27 had large amounts of free pus or cloudy fluid. Ten had small amounts. There were 10 cases with no fluid and 8 cases with walled-off abscess. There were 2 cases not operated upon. A large amount of free pus or cloudy fluid more readily represents a spreading type of peritonitis, especially when there is no walling off, although even this is not always the case. Accordingly, there were cases in which no fluid was present which later died of generalized peritonitis.

In this group of 57 fatal cases, the leucocyte count ranged from 2,360 in a seventy-four-year-old woman who had been ill 2 days, to 42,000 in a twelve-year-old girl, ill 7 days. (There were 9 white counts of 10,000 or less in 55 done.) Most cases were operated upon soon after admission under nitrous oxide oxygen ether. An occasional case was done under spinal anesthesia. There were many complications among these cases. The major complications were peritonitis, paralytic (adynamic) ileus, intestinal obstruction (dynamic), uremia, bronchopneumonia, lobar pneumonia, pelvic abscess, abdominal abscess, pylephlebitis, septicemia, suppurative parotitis, gas bacillus infection, empyema, subphrenic abscess, embolism, fecal fistula, psychosis (attempt at suicide), hemorrhage from abdominal wound, massive intestinal hemorrhage, circulatory collapse, shock, cellulitis of wound, cardiac failure, phlebitis, bed sore, disruption of wound, lung abscess, gangrene of scrotum. We

nondrainage group—a total of 5, or 0.5 per cent. Therefore, fecal fistula may be expected 7 times more frequently when the abdomen is drained. There were 2 cases of bad dehiscence of the wound in the drained group. There was none in the other groups.

We list the more common complications in Table VI.

TABLE VI

	ABDOMEN DRAINED	ABDOMEN NOT DRAINED	SUBFASCIAL DRAIN
Pelvic abscess	33	10	11
Wound infection	100%	128	100%
Fecal fistula	16	4	1
Intestinal obstruction	4	2	0
Paralytic ileus	5	3	1
General peritonitis	5	11	
Lobar pneumonia	10	6	
Bronchopneumonia	15	8	
Embolic deaths	2	0	

Altogether there were, exclusive of wound infections, 139 complications in the drained cases—30 per cent, there were 108 cases with complications exclusive of wound infections in the undrained group—12.5 per cent—less than half as common as in the drained group. In the whole series there were, exclusive of wound infections, which you must remember is of very high incidence, 247 complications, or 18.7 per cent. In other words, the appendectomy is often the easiest part of the procedure in the cases of appendicitis. The early recognition and proper treatment of the complications arising from acute appendicitis tax the ingenuity and ability and wisdom of every surgeon. One out of every 3 cases of appendicitis operated upon has some complication arising. Here is a great field in which to recognize and to treat properly each complication to cut down the mortality. It is easy to see now why operations are always so successful, and yet so many people die of complications. The surgeon who drains an abdomen in acute appendicitis immediately doubles the risk of a complication, aside from trouble with the wound which is nearly always present in some degree. Rather than increasing the life expectancy of the patient, he definitely lowers it.

#### ANALYSIS OF CASES THAT DIED

Of the 57 deaths, 33 were male and 24 female. The youngest was a six-month-old white girl. The oldest stated age was seventy-four years, a white woman. There were 19 patients under fifteen years of age. There were 14 over fifty years and 8 of these over sixty years—a total of 33 in the extremes of life. The duration of the symptoms was up to 1 day, 9 cases; up to 2 days, 12 cases; 2 to 3 days, 17 cases; 3 to 4 days, 4 cases; 4 to 5 days, 2 cases; 5 to 6 days, 3 cases; 6 to 7 days, 6 cases; 10 days, 2 cases; unstated, 2 cases. By far most of the cases had symptoms over 36 hours. Thirty-six cases had symptoms over

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find peritonitis in 20 cases; paralytic ileus, 9 cases; pneumonia and bronchopneumonia, 11; unstated type, 5; pelvic abscess, 6; suppurative parotitis, 4; fecal fistula, 2. Peritonitis, pneumonia, paralytic ileus, and intestinal obstruction were the chief causes of death along with the toxemia that is present in the tremendous infection of the peritoneal cavity.

We believe surgery alone has reached its limit in combating acute appendicitis. Our hope for greater success lies in two directions. Cases must be brought to operation earlier. This problem can be solved by continued education, both of the people at large and of the doctor in general practice. A diagnosis of acute appendicitis in the very early stages is extremely difficult at times, but it is a life saver. We must continue to publicize the dangers resulting from the careless use of cathartics. However, one cannot hospitalize every stomachache. We cannot insist on the removal of every appendix because the total number of people dying from prophylactic appendectomy would easily be greater than the number dying now from acute appendicitis. The chief cause of death in appendicitis is peritonitis and the toxemia arising therefrom and from intestinal obstruction. Early operations will usually prevent these.

#### CONCLUSIONS

1. We have studied 1,325 consecutive cases of acute appendicitis operated upon at Mt. Sinai Hospital from January, 1924, to November, 1935, with a mortality of 4.3 per cent.

2. We feel that the fecalith is directly responsible for a greater virulence of an attack by tending to produce earlier and greater pathologic change although it produced no earlier symptomatology.

3. The mortality is definitely greater in the presence of fecaliths.

4. We have shown that complications occur much more commonly when the abdomen is drained. Of the commonest complications, pelvic abscess is 2 to 4 times as frequent and fecal fistula is 7 times as frequent.

5. When the abdomen is drained, the morbidity is prolonged and mortality is increased.

6. We feel that drainage of the abdomen in acute appendicitis should be sharply restricted to use in localized walled-off abscess.

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# BONE METASTASES FROM CARCINOMA OF THE STOMACH\*

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CARCINOMA of the stomach is the most common cancer of the human body. Metastasis to the surrounding lymph nodes, the liver, and neighboring organs is very frequent and metastasis to the lungs is by no means uncommon. Metastasis to bone, however, is apparently rare and seldom have reports of its occurrence appeared in the literature. Moore,<sup>1</sup> in a study of 1,600 cases of carcinoma of the stomach, found no evidence of bone involvement. Jenkinson<sup>2</sup> found no tumors of the stomach in his series of gastrointestinal malignancies giving rise to bone metastases. In a series of 537 cases of carcinomas of the stomach from Johns Hopkins Hospital, Copeland<sup>3</sup> reports 7 cases with osseous lesions. Southerland<sup>4</sup> states that 1.9 per cent of his 1,032 cases of malignant bony metastases arose from primary growths in the stomach. A higher incidence of 2.5 per cent is given by Matthews,<sup>5</sup> and 5.7 per cent by Warren<sup>6</sup> in their series. Recently, Kerr and Berger<sup>7</sup> reviewed the literature and found 143 cases. To these they added 5 cases, making a total of 148 reported cases.

In a period of fifteen years, from January 1, 1920, to December 31, 1935, 606 patients were admitted to the Presbyterian Hospital upon whom a diagnosis of carcinoma of the stomach was made. Of this group, 10 gave symptoms of bone pains which might be attributable to bone metastases. Roentgenograms were made of the bony structures of these 10 patients and in not a single instance did the x-ray films show any evidence of osseous implants. Autopsies were obtained upon 7 of these 10 patients. In 3 of them metastatic lesions of the bones were found.

## REPORT OF CASES

CASE 1.—Mr. J. F., a carpenter, aged forty-five years, entered the Presbyterian Hospital May 8, 1933, complaining of upper abdominal pain, increasing weakness, and weight loss of twenty pounds during the past four months. Symptoms had been initiated with what he termed a "cold in the stomach" eighteen months previously, followed by increasing periods of epigastric pain and pressure, chiefly after evening meals. Soda had given little relief and induced vomiting had been resorted to with complete relief. Past history was of no importance.

*Examination.*—The patient was a pale, emaciated male whose tongue and skin were dry. His pupils reacted well to light and accommodation. The thyroid gland was of normal size and the cervical lymph glands were not enlarged. Heart and lungs were normal. The blood pressure was 96/68. The abdomen was scaphoid and no peristaltic waves were visible. A firm, fixed, slightly tender mass about 3.5

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cm. in diameter was palpable in the epigastrium. The entire abdomen was soft and no tenderness or abnormal findings were elicited elsewhere. Rectal examination was negative. Reflexes normal.

*Laboratory Findings.*—R.B.C., 3,410,000; W.B.C., 6,600; Hb., 76 per cent. Blood Wassermann and Kahn tests negative. Ewald test meal: total acid, 86; free HCl, 24. Urine normal. Repeated stools showed strongly positive benzidine tests with absence of macroscopic blood. Roentgenograms of the stomach revealed a large filling defect of the antrum extending from the pylorus to well above the angularis.

*Operative Findings.*—At operation, a large carcinoma of the stomach involving the entire pyloric region was found. An extensive resection of the pyloric portion of the stomach and regional lymph nodes was done. No evidence of gross carcinoma remained. Postoperative recovery was uneventful and the patient left the hospital in two weeks.

December 23, 1933, seven months after operation, the patient reentered the hospital because of severe back pain. He had been improving generally until October, 1933, when an attack of dull backache incapacitated him for four days. Following this he had been symptom free until at the onset of an acute cold ten days previously he began to have unbearable back pains. Findings at examination were essentially the same as before except for the following: marked redness of the throat with bilateral cervical lymphadenitis; slight dullness over the left upper chest with few inconstant moist râles; abdomen soft with no palpable masses; marked tenderness, stiffness, and pain on motion of the entire spine. Temperature, 101° F. Pulse, 100. Roentgenograms of the spine showed a slight hipping of the dorsolumbar vertebrae, otherwise no evidence of bone change was seen. The patient rapidly became weaker and both lungs became involved in a terminal pneumonia.

*Autopsy Findings.*—Essential findings were as follows: Extensively resected stomach with freely functioning gastrojejunostomy; carcinomatous metastases of the gastrohepatic, periaortic, abdominal, periesophageal, tracheobronchial, anterior mediastinal, and lower cervical lymph nodes; neoplastic thrombosis of the portal vein; hemorrhagic bronchopneumonia; carcinomatous metastases of the liver and bodies of the dorsolumbar vertebrae and ribs.

CASE 2.—Mr. A. S., a milk-wagon driver, aged fifty-three years, entered Presbyterian Hospital April 19, 1933, complaining of epigastric pain, nausea, vomiting, and loss of weight. Four years previously he had experienced attacks of "indigestion" lasting a few days at a time which completely disappeared after about two months. Fifteen months prior to admission, a sudden return of his epigastric distress occurred and ulcer management was instituted elsewhere. From this he gained some relief, but the pain never completely disappeared. For three months previous to admission he had been having recurrent severe epigastric pain with nausea and vomiting. There was nothing of significance in his past history.

*Examination.*—The patient was anemic and dehydrated. Small bilateral shot-like enlargements of the posterior cervical lymph glands were palpable. The pupils were small and reacted to light and accommodation. The thyroid gland was not enlarged. Heart and lungs were normal. Blood pressure 110/70. Pulse 64. In the epigastrium a small slightly tender mass could be palpated. The liver, spleen, and left kidney were not palpable. The right kidney was normal. The rectum and prostate were normal. Reflexes normal.

*Laboratory Findings.*—R.B.C., 3,500,000; W.B.C., 7,200; Hb., 42 per cent. Blood Wassermann and Kahn tests negative. Ewald test meal: total acid, 85; free HCl, 9. Lactic acid bacilli were present in numbers. Urine normal. Stools were brown colored and contained marked chemical blood. Roentgenograms of the

stomach revealed a large filling defect extending from the pylorus along the lesser curvature to above the angle of the antrum.

*Operative Findings.*—At operation, an extensive carcinoma of the prepyloric portion of the stomach was found. The growth extended midway up the stomach. Regional lymph glands along the entire lesser curvature were involved. An extensive resection was done removing all the stomach to within a few centimeters of the esophagus. The patient made an uneventful recovery.

Nine months after operation the patient suddenly began a rapid loss of weight and developed pain in the back between the shoulders which extended down the spine and became quite severe. He was readmitted to the hospital February 3, 1934. On examination, the findings were essentially as before, except for marked tenderness over the dorsal and lumbar spine with considerable pain and limitation of motion. The abdomen was soft with no evidence of carcinomatous recurrence. Roentgenograms of the dorsal and lumbar spine showed no evidence of bone changes. The patient continued to lose weight rapidly, became weaker, and died of a pneumonia with carcinomatous metastases in both lungs.

*Autopsy Findings.*—These were essentially as follows: Resected distal end of the stomach with a freely patent gastrojejunostomy; carcinomatous metastases of the mesenteric and periaortic abdominal lymph nodes; carcinomatous metastases of the lungs and tracheobronchial lymph nodes; extensive carcinomatous metastases of the bodies of the dorsolumbar vertebrae, manubrium sterni, and ribs.

CASE 3.—Mr. A. E., an engineer, aged forty years, entered the Presbyterian Hospital September 11, 1935, complaining of epigastric distress, anorexia, and loss of weight for one year. Back pain had been present for five days. Accompanying the epigastric distress there had been nausea during the last two months and on several occasions vomiting had occurred. The back pain had been constant for five days and extended over the dorsal, lumbar, and sacral spine. He had been under the care of a doctor who, without x-rays or gastric analysis, had made a diagnosis of peptic ulcer and had treated the patient with alkaline powders and a milk diet. His symptoms had become progressively worse on this regime and the sudden back pain brought him into the hospital. His past history was of no importance.

*Examination.*—The patient had a marked pallor and apparently was having considerable pain. Pupils were small and reacted well to light and accommodation. There was moderate lymphadenopathy in both anterior triangles of the neck without tenderness. The thyroid gland was not enlarged. Heart and lungs were normal. Blood pressure, 120/76. Pulse, 100. The abdomen was soft. In the epigastrium there was moderate tenderness on deep palpation. No masses could be found. The liver and spleen were not palpable and the kidneys were of normal size and without tenderness. Reflexes were normal. Rectal examination revealed a soft prostate of moderate size with no tenderness. The spine was tender on percussion over the dorsolumbar region. Mobility was not limited on slow motion, although considerable pain was elicited. A neurological examination revealed no abnormal findings of the nervous system.

*Laboratory Findings.*—R.B.C., 2,940,000; W.B.C., 5,450; Hb., 47 per cent. Blood Wassermann and Kahn tests negative. Ewald test meal: total acid, 28; free HCl, 12. Urine normal. Repeated stool examinations showed no macroscopic but marked chemical evidence of blood. In roentgenograms of the stomach, a deformity of the lesser curvature could be seen, extending high on the posterior wall. Roentgenograms of the spine showed no evidence of bone change.

*Autopsy Findings.*—Essential findings were an ulcerative adenocarcinoma of the lesser curvature of the stomach with metastases to the perigastric, periaortic abdominal lymph nodes, and to the dorsolumbar spine.

## DISCUSSION

To further confirm our negative findings in x-rays of the skeletal structures taken during the lives of these patients, we again x-rayed the bones in which gross metastatic lesions had been found at autopsy.

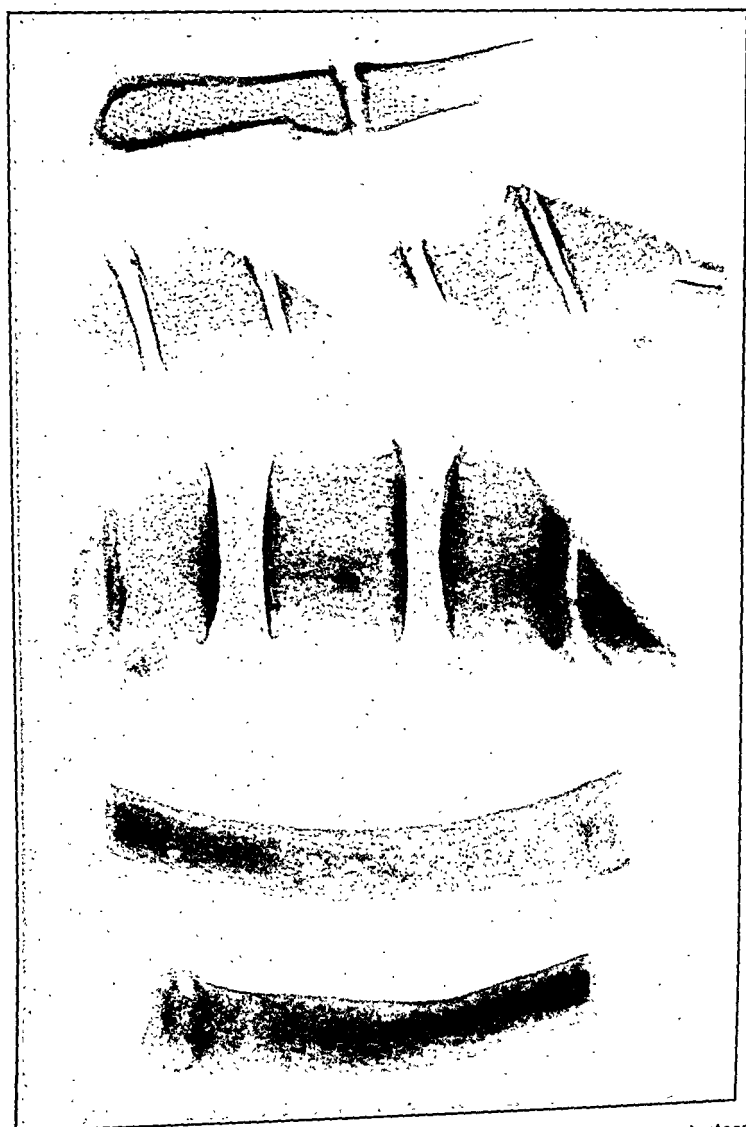


Fig. 1.—X-rays made after removal of bones, failing to show gross metastases.

With all obscuring shadows removed and a maximum of detail present, we were still unable to see any evidence of secondary growths in these x-rays (Fig. 1). Although metastasis to bone from primary carcinoma of the stomach is not common, it probably occurs more fre-

quently than is usually supposed. While secondary bony lesions may be suspected and searched for on the basis of clinical symptoms, if the roentgenograms fail to show the presence of gross lesions, as they have in our cases, many diagnoses must remain questionable or unconfirmed unless autopsy is permitted.

From the series of cases reported in the literature where the type of metastases has been noted, osteoplasia and osteoclasia have occurred in about equal numbers. Both types of change have been observed in the same individual. Few writers have expressed an opinion regarding the relation of the size, location, and type of the gastric lesion to the

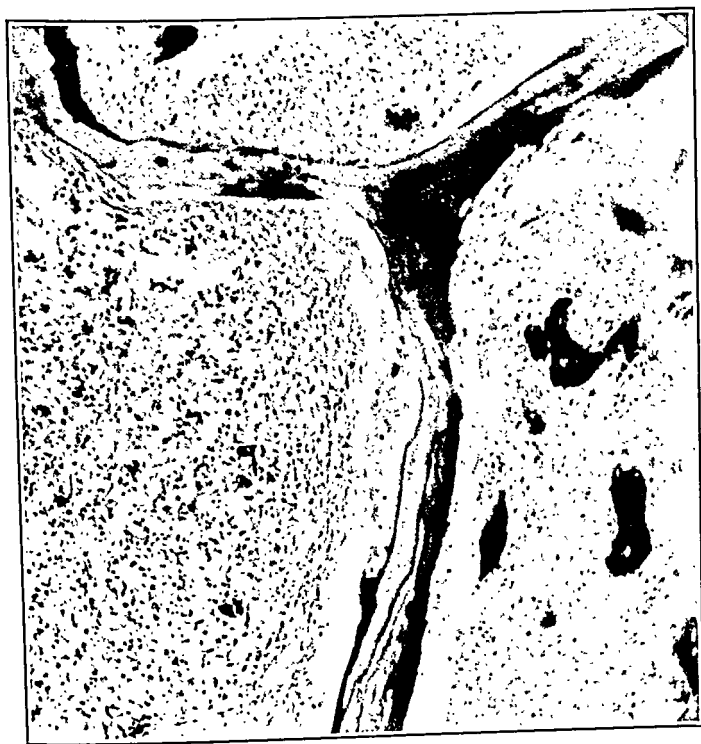


Fig. 2.—Microscopic section showing carcinomatous implants with absence of osteoplasia and osteoclasia.

osseous metastases. After a study of the recorded cases, Kerr and Berger are of the opinion that the size of the primary lesion, its site, and general type have no bearing on the probable occurrence of metastasis to bone. The primary growths in our three cases were extensive adenocarcinomas involving the prepyloric regions and a great part of the lesser curvatures. The metastatic growths to bone all gave the same gross and microscopic appearance. On cross-sections of the vertebrae were mosaic patterns of dark purple and opaque yellow-gray areas about equal in distribution. Microscopically, carcinomatous tissue was implanted between the trabeculations of the skeletal struc-

tures and very little osteoplasia or osteoclasia had taken place (Fig. 2). The fact that metastasis had taken place by filling the spaces of the bony meshwork without causing noticeable destruction or proliferation of bone is undoubtedly the reason for failure of the x-rays to reveal the presence of tumor growths.

#### SUMMARY

1. Bony metastases from carcinoma of the stomach are rare, Kerr and Berger having been able to collect only 143 cases from the literature.

2. In a study of 606 cases of carcinoma of the stomach, 3 cases of proved bony metastases have been found.

3. Roentgenograms failed to show the presence of metastatic lesions in the 3 cases here reported, due to the absence of either osteoplastic or osteoclastic changes in the involved bones.

4. Bony metastases from carcinoma of the stomach may be more common than has been supposed. *Diagnosis must depend entirely on clinical symptoms, where roentgenograms fail, and consequently cannot be confirmed in cases where necropsy is refused.*

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## THE EFFECT OF CARBON ARC RADIATION ON WOUND HEALING

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THE influence of radiant energy on wound healing has been recently reviewed by Laurens<sup>1</sup> and Arey.<sup>2</sup> Many of the leading European heliotherapists, including Bernhard and Rollier, have extolled the merits of sunlight, both natural and artificial, and report marked benefit following its use, particularly in refractory wounds. Goldammer<sup>3</sup> found that the results were brilliant both in fresh and granulating wounds received in battle. Coulter and Smith<sup>4</sup> likewise think ultraviolet radiation of definite value in the treatment of wounds. Some workers,<sup>5, 6</sup> however, have found that healing is not hastened by artificial radiant energy. Coburn and Cowles<sup>7</sup> not only failed to find any benefit on treating a large series of rats by irradiation with carbon and iron arcs, but their work seemed to indicate a retarding effect. Pollaczek<sup>8</sup> found that doses slightly over optimal produced injurious effects.

Adult healthy dogs of medium size (5 to 8 kg.) with pink skin and white or light colored coats were used. The wounds were made in pairs, one on each side of the body in the saddle region and were as identical as possible, the left wound being the experimental while the right served as the control. The wounds were of two sizes, 18 and 40 mm. in diameter (255 and 1256 sq. mm.) and of skin depth. They were made with sharp cork borers placed firmly on the skin and rotated. This method prevents reflex contraction and results in round wounds with well-defined margins. Because of their position the wounds remained clean without bandaging and the animals could not lick them.

The wounds were measured at intervals throughout the healing period by placing a clean glass plate over them and tracing the periphery with a sharp pointed glass pencil, transferring this to paper and determining the area with a planimeter. Healing was considered complete when the scab fell off or could easily be brushed off leaving a dry cicatrix beneath.

Irradiation was begun one to three days following the operation. The animals were placed in a hammock so adjusted under their bodies as to allow them to stand or to rest in the supports during the irradiation. The conditions were varied in different groups by varying the duration of the exposure, the number of exposures per week, the dis-

tures and very little osteoplasia or osteoclasia had taken place (Fig. 2). The fact that metastasis had taken place by filling the spaces of the bony meshwork without causing noticeable destruction or proliferation of bone is undoubtedly the reason for failure of the x-rays to reveal the presence of tumor growths.

#### SUMMARY

1. Bony metastases from carcinoma of the stomach are rare, Kerr and Berger having been able to collect only 143 cases from the literature.

2. In a study of 606 cases of carcinoma of the stomach, 3 cases of proved bony metastases have been found.

3. Roentgenograms failed to show the presence of metastatic lesions in the 3 cases here reported, due to the absence of either osteoplastic or osteoclastic changes in the involved bones.

4. Bony metastases from carcinoma of the stomach may be more common than has been supposed. Diagnosis must depend entirely on clinical symptoms, where roentgenograms fail, and consequently cannot be confirmed in cases where necropsy is refused.

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TABLE I

SMALL WOUND EXPERIMENTS (LEFT WOUND IRRADIATED, RIGHT WOUND CONTROL)

EXPERIMENT NUMBER	IRRADIATION PROCEDURE	TOTAL RADIANT ENERGY RECEIVED IN GM. CALORIES PER SQ. CM.	HEALING TIME IN DAYS		DIFFERENCE
			LEFT	RIGHT	
1	Entire side for 10 minutes 3 times per week at 1 M.	38.0	25	25	0
2	Entire side for 10 minutes 3 times per week at 1 M.	33.3	21	21	0
3	Entire side for 10 minutes 3 times per week at 1 M.	38.0	22	26	+4
4	Entire side for 10 minutes 3 times per week at 1 M.	57.0	31	35	+4
5	Entire side for 10 minutes 3 times per week at 1 M.	52.3	28	28	0
6	Entire side for 10 minutes 3 times per week at 1 M.	71.3	29	25	-4
7	Entire side for 15 minutes 3 times per week at 1 M.	71.3	24	24	0
8	Entire side for 15 minutes 3 times per week at 1 M.	64.1	25	23	-2
9	Entire side for 15 minutes 3 times per week at 1 M.	57.0	21	21	0
10	Entire side for 15 minutes 3 times per week at 1 M.	71.3	24	25	+1
11	Entire side for 15 minutes 3 times per week at 1 M.	95.0	33	33	0
12	Entire side for 15 minutes 3 times per week at 1 M.	85.5	32	36	+4
13	Entire side for 15 minutes 3 times per week at 1 M.	78.4	26	26	0
14	Entire side for 15 minutes 3 times per week at 70 cm.	87.3	21	19	-2
15	Entire side for 15 minutes 3 times per week at 70 cm.	116.4	24	24	0
16	Entire side for 15 minutes 3 times per week at 70 cm.	145.5	31	36	+5
17	Entire side for 15 minutes 3 times per week at 70 cm.	130.9	28	28	0
18	Entire side for 15 minutes 3 times per week at 70 cm.	101.9	17	33	+16
19	Entire side for 15 minutes 3 times per week at 70 cm.	116.4	22	21	-1
20	Entire side for 15 minutes 3 times per week at 70 cm.	130.9	24	24	0
21	Entire side for 15 minutes 3 times per week at 70 cm.	87.3	18	20	+2
22	Entire side for 15 minutes 3 times per week at 70 cm.	145.5	34	29	-5
23	Entire side for 15 minutes 3 times per week at 70 cm.	101.8	22	22	0
24	Entire side for 15 minutes 3 times per week at 70 cm.	145.5	22	22	0
25	Entire side for 15 minutes 3 times per week at 70 cm.	116.4	25	22	-3
26	Entire side for 15 minutes 3 times per week at 70 cm.	145.5	24	23	-1
27*	Wound (locally) for 15 minutes 3 times per week at 70 cm.	58.2	17	17	0
28*	Wound (locally) for 15 minutes 3 times per week at 70 cm.	145.5	22	20	-2
29*	Wound (locally) for 15 minutes 3 times per week at 70 cm.	101.9	16	20	+4

\*Animal kept in complete darkness except when irradiated.



tance from the arc; by irradiating the whole left side of the animal or just the wound (local irradiation), by keeping some of the animals in complete darkness between irradiations, and by not irradiating some at all.

The source of radiant energy was a carbon arc lamp burning "sunshine" carbons, operated at between 24 and 27 amperes and with a potential drop across the arc of 50 to 60 volts. The total energy emitted was 0.475 gm. calories per square centimeter per minute at 1 M. distance, with a percentage distribution of ultraviolet 3, luminous 23.5, and infra-red 73.5.

#### COMMENT

Table I summarizes the 29 small wound (255 sq. mm.) experiments. They can be divided into four groups. In the first three groups the whole side of the animal was irradiated with progressively increasing doses per group, while in the fourth group the exposure was limited to just the wound (local irradiation), the rest of the body being shielded from radiation. Since it seemed possible that the animals might be obtaining sufficient radiation between exposures to influence the healing time of the wounds, particularly the controls, these animals were also kept in complete darkness between treatments.

In 8 of the 29 experiments the irradiated wound healed more quickly and in 8 less quickly than the control, while in 13 there was no difference. In only one experiment (No. 18) was the acceleration in healing rate marked.

Since the results on the small wounds were indecisive, an attempt was made, in the second series, to obtain more definite results by using a larger wound (1,256 sq. mm.), thus prolonging the healing time and allowing the radiant energy more time to manifest its effects.

Table II summarizes all of the large wound experiments. Irradiation procedures similar to those for the small wounds of Table I were used. One group, however (Experiments 38 through 45), was given more frequent but shorter irradiations to more nearly simulate natural radiation. In 10 of the 19 large wound experiments, the irradiated wound healed more quickly and in 4 less quickly than the control, while in 5 there was no difference. In 2 experiments (Nos. 33 and 40) there was a marked and in 2 (Nos. 30 and 31) there was a moderate acceleration while in 1 (No. 32) there was a moderate retardation in the healing rate of the irradiated wound.

Table III summarizes 5 experiments with small wounds and 7 experiments with large wounds in which no carbon arc radiation was administered. Of the 5 small wound experiments, only 1 slight difference in healing time was noted. Of the 7 large wound experiments, 4 showed a difference in healing time, 3 of which were but slight while

experiments. Groups 46 through 48 also received the same amount of radiant energy locally per unit time and were also kept in the dark between treatments to more specifically irradiate the experimental wound. Though all three showed positive effects none of the differences were marked.

TABLE III  
NONIRRADIATION EXPERIMENTS

EXPERIMENT NUMBER	SMALL WOUNDS			EXPERIMENT NUMBER	LARGE WOUNDS		
	HEALING TIME IN DAYS LEFT	HEALING TIME IN DAYS RIGHT	DIFFERENCE		HEALING TIME IN DAYS LEFT	HEALING TIME IN DAYS RIGHT	DIFFERENCE
49	24	24	0	54	35	39	4
50	29	29	0	55	42	37	5
51	28	28	0	56	38	41	3
52	34	31	3	57	43	43	0
53	27	27	0	58	28	28	0
				59	29	29	0
				60	46	55	9

The average healing time of the 10 nonirradiated small wounds (Table III, left) was 28.1 days; of the 29 directly irradiated small left wounds (experimental) (Table I), 20.9 days; and of the 29 indirectly irradiated small right wounds (control) (Table I), 21.7 days. A similar comparison of all the large wounds shows an average healing time for the 14 nonirradiated wounds (Table III, right) of 38 days; for the 19 directly irradiated left wounds (Table II) of 33.5 days; and for the 19 indirectly irradiated right wounds (Table II) of 35.8 days. This indicates a mild acceleration in the healing rate of the wounds in the irradiated animals, the indirectly irradiated right wounds, which received only the general systemic effect, showing relatively less acceleration than those directly irradiated.

#### SUMMARY

The rate of healing of 60 pairs of experimental wounds in dogs has been studied. In 48 of the experiments (29 small, 255 sq. mm.; and 19 large, 1,256 sq. mm.), the left wound was irradiated with a carbon arc lamp. Various amounts of radiant energy were given in different groups. In some the entire side of the body, in others only the wound was irradiated. Some of the animals were kept in complete darkness between irradiations.

In the 29 small wound experiments, 8 of the irradiated wounds showed acceleration, 8 retardation, and 13 no difference in healing rate when compared to its control.

Of the 19 large wound experiments, 10 showed acceleration, 4 retardation, and 5 no difference in healing rate when compared to its control.

the fourth (No. 60) showed a difference of nine days. This difference of nine days is exceeded by only 3 of the irradiation experiments (Nos. 18, 33, and 40) and equalled by 1 (No. 30).

The variability of the results in all groups makes them difficult to evaluate. No one of the irradiation procedures can be selected as being definitely superior. Groups 30 through 33 showed 3 well-benefited wounds and 1 (No. 32) that was definitely retarded. The same amount of radiant energy per unit time, administered locally, in Groups 34 through 37, showed no difference in healing time in the four

TABLE II  
LARGE WOUND EXPERIMENTS  
(LEFT WOUND IRRADIATED, RIGHT WOUND CONTROL.)

EXPERIMENT NUMBER	IRRADIATION PROCEDURE	TOTAL RADIANT ENERGY RECEIVED IN CM. CALORIES PER SQ. CM.	HEALING TIME IN DAYS		DIFFERENCE
			LEFT	RIGHT	
30	Entire side for 15 minutes 3 times per week at 70 cm.	145.5	28	37	+9
31	Entire side for 15 minutes 3 times per week at 70 cm.	174.6	32	38	+6
32	Entire side for 15 minutes 3 times per week at 70 cm.	232.8	38	32	-6
33	Entire side for 15 minutes 3 times per week at 70 cm.	189.5	31	45	+14
34	Wound (locally) for 15 minutes 3 times per week at 70 cm.	130.9	27	27	0
35	Wound (locally) for 15 minutes 3 times per week at 70 cm.	160.0	29	29	0
36	Wound (locally) for 15 minutes 3 times per week at 70 cm.	174.6	29	29	0
37	Wound (locally) for 15 minutes 3 times per week at 70 cm.	174.6	38	38	0
38	Wound (locally) for 5 minutes 6 times per week at 70 cm.	145.5	36	35	-1
39	Wound (locally) for 5 minutes 6 times per week at 70 cm.	116.4	28	33	+5
40	Wound (locally) for 5 minutes 6 times per week at 70 cm.	130.9	35	46	+11
41*	Wound (locally) for 5 minutes 6 times per week at 70 cm.	116.4	28	28	0
42*	Wound (locally) for 5 minutes 6 times per week at 70 cm.	140.6	31	33	+2
43*	Wound (locally) for 5 minutes 6 times per week at 70 cm.	160.1	38	41	+3
44*	Wound (locally) for 5 minutes 6 times per week at 70 cm.	150.4	39	34	-5
45*	Wound (locally) for 5 minutes 6 times per week at 70 cm.	169.8	46	43	-3
46*	Wound (locally) for 15 minutes 3 times per week at 70 cm.	160.1	32	36	+4
47*	Wound (locally) for 15 minutes 3 times per week at 70 cm.	180.2	31	33	+2
48*	Wound (locally) for 15 minutes 3 times per week at 70 cm.	217.4	40	44	+4

\*Animal kept in complete darkness except when irradiated.

## Editorials

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### The Surgical Treatment of Carcinoma of the Breast

ONE of the more interesting developments in surgical therapy during the last decade or so is the apparent casualness of many operators in regard to the radical removal of the breast in cases of carcinoma of that organ. This rather nonchalant attitude varies from the performance of, a mere local excision of the malignant tumor itself, a simple mastectomy, or a hurried inadequate and incomplete dissection of the chest wall and corresponding axilla. When questioned as to the reason for this relaxation from the rigid technique of meticulous and radical extirpation of the breast and its contiguous structures, the various surgeons will make the rather naïve reply that "the operation is less mutilating and besides radiation therapy will take care of local recurrences!" The question of the efficacy of pre- or post-operative radiation therapy in the treatment of malignant tumors of the breast has nothing whatever to do with the proper or improper *surgical* care administered to a patient affected with such a tumor. In our present state of knowledge radiation therapy, either deep x-ray or radium, although a most important adjunct, does not justify the slightest lessening in the thoroughness or the radicalness of the operative removal of the malignant breast with its associated structures of the pectoral and corresponding axillary regions. The diffusion of information concerning breast tumors through the lay press and periodicals has made it possible to see these cases at such an early stage of the disease that a definite preoperative diagnosis often cannot be made, thus never before has the opportunity for the success of the surgical cure of this malady been so favorable or opportune. The general characteristics and technique of the operation for the radical amputation of the breast have been developed over a period approximating one hundred years and this operation today may be considered, more than almost any other in surgery, one that is standardized. Years of clinical, pathologic, and surgical research revealing the clinical course of this disease, its paths of invasion in the breast and its surrounding structures, the location and frequency of its metastases, implantations and recurrences, the method of operating from the simplest and most conservative to the most radical removal, have all played an important rôle in the development of this universally recognized surgical procedure. It is certainly one operation upon which the majority of well-trained, thinking surgeons are in full agreement

In 5 small wound experiments in which no carbon arc radiation was given, only 1 slight healing time difference was found. In 7 large wound nonirradiation experiments, 4 showed slight to moderate differences.

#### CONCLUSION

Carbon arc irradiation, of the type and dosage used, has but little accelerating effect on the healing of clean wounds in the dog.

This study was suggested to me by Prof. Henry Laurens.

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subdivide, and acquire a lumen at their expanded distal ends, thus giving rise to the systems of ducts and lobules of immature gland tissue. With the further development of the latter, the surrounding mesoblastic stroma is broken up into the interlobular septa and fibrous framework of the corpus mammae. Naturally, the lymphatic vessels which develop simultaneously with the gland parenchyma accompany the downgrowth of the original ectoblastic pouch and thus the deeper lymph vessels surround the groups of alveoli as channels that lie within the interlobular connective tissue and pass toward the surface where they form the rich subareolar plexus. The latter also receives the collecting stems from the close cutaneous networks that drain the integument covering the nipple, areola, and the skin overlying the dome of the breast. In addition to a few trunks that follow the perforating arteries and become afferents of the lymphatic nodes lying along the internal mammary artery, all the lymphatics of the breast join to form two or three large trunks that pass from the lower and lateral borders of the organ through the subcutaneous tissue toward the axilla to empty into the axillary glands.

It would seem possible that the most important tissue to remove in a radical amputation of the breast is the skin. This reasoning is based upon the anatomic facts mentioned above. The basin, so to speak, which receives the greatest lymph drainage from the breast is the subareolar and subcuticular plexus underlying the skin covering the dome of the breast. The breast is an appendage of the skin and the first spread of carcinomatous cells will be along the lymphatic channels toward the subareolar plexus. A resection of skin theoretically as extensive and wide as that of the underlying muscle and fascia layers would be ideal but, of course, impractical; yet the least that should be done is the complete removal of the entire skin covering the dome of the breast. In addition, the circular incision should be extended sufficiently to include the newgrowth and not the nipple as the center of the circle. The most important by far of the three layers of tissue, i.e., skin, fascia, and muscle, is unquestionably the skin. When a local recurrence takes place in the skin, it means the disease has persisted uninterruptedly since before operation and that either the operator did not get beyond it at the time of operation and cut through the growth or that the tumor had grown further in the skin than he anticipated. In either event his margin in the skin was too narrow and the new manifestation of the tumor is merely a persistence of a growth that was there at the time of operation and not a recurrence of the disease at some period following operation. Even a cursory examination of the skin incisions used today that will allow the operator to close the operative defect after removal of the breast show that the amount of skin sacrificed is totally inadequate. In the

the world over; and yet, paradoxical as it may seem, this operative procedure today is, generally speaking, not carried out or performed as well as it was twenty years ago. One reason for this regression of the operative procedure would seem to be due to a total lack of conception of the true principles upon which the surgical attack is based and the ends it is supposed to attain and/or a lack of technical ability on the part of the surgeon. After all the operation is a surface one which, because of the low mortality associated with it, may be performed in any sort of an offhand, least troublesome manner, the operative field being covered, in the majority of instances, with skin flaps which heal up promptly and thus conceal all evidence of a lack of thoroughness and incompetence at the time of operation. It would, of course, be impossible to prove that a more careful operation, in an individual instance, would have prevented a local return of the disease, but it can be stated without reservation that the percentage of local recurrence of this malady is far less in the hands of those surgeons who take pride in the perfection of their dissections in these cases. The operator should be held responsible only for the postoperative recurrence of the disease within the local limits of the operative field and not for remote metastases. All that can be expected of such an operation is to remove and cure the disease locally and this would seem to be the only yardstick by which one can measure the success or failure of any surgeon attempting to treat malignant tumors of the breast.

In the reports of postoperative studies published by many different observers in this country and abroad, the majority of local recurrences following radical amputation of the breast have taken place at some point within the skin overlying the operative field. When one considers the embryologic development of the breast, together with the arrangement, location, and drainage of the lymphatic capillaries in the skin and into the subcuticular lymphatic plexus, it is not to be wondered that so many recurrences take place in the skin. The mammae are ectodermal in origin growing from a knoblike thickening of ectoblast of the embryo down into the underlying mesoblastic tissue. This ectoblastic ingrowth represents a sunken area of integument that in principle corresponds to the marsupial pouch of the lowest mammals (monotremes). Solid epithelial sprouts grow out from the sides of the conical- or flask-shaped epidermal plug and are the first anlagen of the true mammary gland, later becoming the excretory ducts. Subsequently the central part of the ectoblastic ingrowth undergoes degeneration and destruction, and what at first was an elevation now becomes a depression of the surface. From the middle of this depressed area there appears about the time of birth an elevation that later becomes the nipple. Meanwhile, the epithelial duct outgrowths penetrate the surrounding condensed mesoblastic stroma, increase in length,

nificance of this accidental discovery is that such blood can be conserved without the addition of an anticoagulant. Under aseptic precautions from 2 to 3.5 liters of blood is obtained from the jugular veins of each cadaver and after necessary bacteriologic and serologic tests have been done, the blood is hermetically sealed and stored at a temperature not greater than 4° C. Because fragility of the red blood cells with subsequent hemolysis increases markedly after the tenth day, it is rarely used after this period.

According to these investigators, experience in over 1,000 cases has demonstrated that these transfusions can be done with comparative safety. The Russian advocates further claim that in addition to its economic advantages emergency transfusions can always be easily and quickly performed. However, it is of interest that they do not advocate replacing present-day methods by this procedure. Further analysis of their 1,000 cases reveals the disturbing fact that the incidence of reactions was 21 per cent and fatalities 0.7 per cent. At present any method of transfusion which gives untoward reactions in over 1 per cent of the cases should not be considered sufficiently developed for universal adoption. Whereas such a method may have economic advantages in Soviet Russia, at the present time justification of its use here can hardly be considered warranted. However, it promises a fruitful field of utilization during warfare.

Whereas in this country a somewhat parallel method has been developed, the blood is obtained from living donors. The method consists essentially of withdrawing approximately  $\frac{1}{2}$  liter of blood from every suitable patient and visiting relatives in the hospital, adding citrate solution as an anticoagulant, and after proper serologic and bacteriologic examinations "depositing" it in the "blood bank." Withdrawals are then made against each "ward account" as the necessity arises. Whereas the transfusion of conserved blood may be considered justifiable and therapeutically advantageous in large charitable institutions, such a method, because of its departure from the physiologic ideal, can never displace the transfusion of unmodified blood.

—*Michael DeBakey, M.D.*  
New Orleans, La.



line of the incision above and below the tumor the elliptical area of skin removed is perhaps sufficient; but on the sides, in order to bring the skin flaps together, the margin is far too small. The great frequency of the postoperative out-cropping of the disease along the line of the incision bears ample witness to this error.

Emphasis should be laid upon the point that the layer of skin is the most vital to the ultimate success or lack of it following radical amputation of the breast for a malignant tumor, and further that this layer of integument should be removed thoroughly and radically without the slightest regard by the operator for closure. The remaining defect can be covered by skin grafts either at the time of operation with Thiersch grafts, or, in the event that the operator is not acquainted with the technique of cutting these, small Revenolin grafts may be placed upon the granulating wound some days later. The importance of a wide excision of the skin has never been sufficiently emphasized, although Halsted taught and wrote about this feature continuously during his lifetime. It is important to realize that the skin cannot be thought of as an outer garment existing merely to cloak the operative field and to be cut accordingly in order to fit as perfectly as possible; but on the contrary it must be regarded as a dangerous infested maze of potential disease to be got rid of with no thoughts of closure or cosmetic results. Lack of patience to learn how or to perform a meticulous dissection in the execution of a radical extirpation of the breast, speed in operating because of the feeling that to be slow and careful is to be considered somewhat less dexterous, and finally being concerned about short postoperative hospitalization, avail patients very little solace when the one chance they had to be rid of their disease has been sacrificed because of ignorance or carelessness or both.

—William F. Riehoff, Jr.

### **"Canned" Blood Transfusion**

**T**HERE is probably no other place in the world today where blood transfusion is being more extensively studied than in Soviet Russia. From these intensive investigations there has recently emerged the practice of transfusing stored cadaver blood. Whereas previously blood from all healthy "donors" was employed, more recently it has been found that the more suitable cadavers are those of persons dying suddenly; for example, as a result of coronary thrombosis, electrocution, cerebral hemorrhage, or traffic accidents. This is due to the curious but unexplainable phenomenon that, whereas such blood rapidly coagulates if removed in the first few hours after death, in from one-half to one and one-half hours it "disagulates" by supposedly undergoing fibrinolysis and remains fluid. The practical sig-

the different parts of the prostate is known. The knowledge of these effects might be helpful in judging the benefits to be derived from hormonal therapy in prostatic hypertrophy.

A definite pituitary hypertrophy follows castration. Korenchevsky and coworkers and McCullagh and Walsh found that injections of male hormone restored the prostate to normal but did not control the pituitary hypertrophy in castrates. The latter investigators also found that if a castrated and a normal animal, usually the rat, were joined in parabiosis, and if then a testicular mush was injected into the castrated partner, pituitary activity was controlled and one did not find prostatic enlargement in the normal animal. In control experiments where a castrated rat was united in parabiosis with a normal animal, prostatic hypertrophy, as determined by glandular weight, resulted in the normal partner (McCullagh and Walsh). From these and other experiments, McCullagh and coworkers evolved the hypothesis that the internal secretion of the testis is of a dual nature. One substance extracted by organic solvent and believed to have its origin in the interstitial tissue is called androgin; the other substance, which is water soluble and supposed to be secreted by the cells of the seminiferous tubules, has the properties of an inhibiting chalone and is called inhibin.

The results of Lower and others suggest that the injection of the lipid-soluble fraction of the testis into a normal rat causes hypertrophy of the prostate, while the injection of the water-soluble extract causes atrophy of the gland.

#### THE EFFECT OF THE PITUITARY GLAND ON THE TESTIS AND PROSTATE

Following hypophysectomy there is atrophy of the testis and accessory sex glands which can be completely repaired by reimplantation or injection of pituitary substance (Smith and Engle, Evans and Simpson). Adequate doses of male sex hormone will prevent atrophy of the accessory sexual organs in hypophysectomized as well as in castrated rats (McCullagh and Walsh, Zuckerman and Parkes). Urinary androgens will maintain the normal appearance of the testis in hypophysectomized rats; pituitary extracts, the pituitary-like hormones from the urine and yeast, will do the same thing. If there is already atrophy of the rat testis following hypophysectomy, urinary androgens will not repair this degeneration; however, pituitary extracts will restore the appearance of the atrophic gonad to normal (Martins and Rocha, Hisaw, Nelson, Leonard, McCullagh).

From the results of injecting anterior pituitary-like substance and parabiosis experiments, it is known that pituitary hyperfunction may cause prostatic hypertrophy (McCullagh and Walsh). The best evidence of pituitary hyperfunction that is known to date is the presence of the gonadotropic hormone in the urine. There are at least six sources

mones has often been more confusing than enlightening. The first step in the elucidation of this relationship is the separation of the component hormones.

1. *Testicular Hormones*.—While Berthold in 1849 demonstrated that the testis had an internal secretion, it was not until 1927 that the first successful extraction of a hormone from testicular tissue was performed (McGee). Butenandt in 1931 crystallized the male hormone, androsterone, from human urine; in 1934, Ruzicka synthesized androsterone from cholesterol. Another male hormone, testosterone, was prepared from fresh testicular tissue by Laqueur and coworkers in 1935; this same substance and others with androgenic activity have been synthetically prepared. It is known that the chemical and experimental properties of testosterone and androsterone are different. The number and specific nature of other male hormones are unknown. (See reviews of Koch and of Moore and Price.)

2. *Hypophyseal Hormones*.—From the work of Aschheim and Zondek, Smith and Engle, Evans and others, at least two gonadotropic hormones of pituitary origin are known. One causes maturation of the ovarian follicle, with the resultant production of the ovarian hormone, theelin, which prepares the uterine mucosa for the reception of the ovum. The other causes luteinization of the remains of the ruptured ovarian follicle, the corpus luteum, which in turn secretes a hormone, progestin, causing growth of the fertilized ovum, decidual and placental formation. In pregnancy, a hormone, prolactin, closely resembling the second gonadotropic hormone of the pituitary, is secreted in the urine together with theelin.

In the male rat, Hisaw and others found that the follicle stimulating hormone stirred proliferation of the germinal epithelium alone, while the luteinizing hormone acted in the interstitial cells and caused enlargement of the accessory sex organs, apparently through the male sex hormone secreted by the hypertrophied interstitial tissue. The enlargement was intensified by the simultaneous action of the two hormones. Recently Evans and his associates described the separation of a third gonadotropic hormone which stimulates the Leydig cells of the testis. The importance of this possible hormone in explaining hypertrophy of the prostate will be discussed later.

3. *Prostate*.—No definite prostatic hormones have been isolated.

#### EFFECT OF MALE HORMONE ON THE PROSTATE AND THE HYPOPHYSIS

Castrates have underdeveloped prostates; to bring about maximal reduction in size of this gland, castration must be performed early in life. MacCallum points out that neither the effect of castration on the different lobes of the prostate and the accessory periurethral, subcervical, or trigonal glands, nor the effect of the internal secretion of the testis on

the different parts of the prostate is known. The knowledge of these effects might be helpful in judging the benefits to be derived from hormonal therapy in prostatic hypertrophy.

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From the results of injecting anterior pituitary-like substance and parabiosis experiments, it is known that pituitary hyperfunction may cause prostatic hypertrophy (McCullagh and Walsh). The best evidence of pituitary hyperfunction that is known to date is the presence of the gonadotropic hormone in the urine. There are at least six sources

of gonadotropic hormone: (1) the anterior lobe of the pituitary; (2) prolan or the anterior pituitary-like substance of pregnancy urine; (3) urine of men with testicular tumors (Aschheim and Zondek, Ferguson, and Hinman); (4) the urine of male castrates; (5) urine of some cryptorchids (Hess and others); and (6) urine of some normal men (cyclic) (Harris and Brand). Whether these hormones are one and the same has been debated (see Hinman's review).

Castrates, although showing gonadotropic substance in the urine, do not have prostatic hypertrophy as there is no testicular tissue to act as an intermediary. The question arises: Do patients with malignancy of the testis with gonadotropic hormones in the urine have enlargement of the prostate? Teems found three cases of interstitial cell tumor of the testis associated with either normal or atrophic prostatic gland and a case of carcinoma of the "genitaloid" cells of the testis accompanied by practically an absence of interstitial cells in a man sixty-five years of age with a hypertrophied prostate. There is no mention of the presence or absence of gonadotropic substance in the urine of these patients. Ferguson in 1933, in a study of 117 cases of teratoma testis, noted diffuse enlargement of the prostate of seminal vesicles accompanied by hyperplasia of the interstitial cells of the opposite testicle, varying in degree with the amounts of anterior pituitary-like substance recovered from the urine. As Geschiekter points out, however, clinical hypertrophy of the prostate is usually focal rather than diffuse; therefore, it cannot be assumed that hormonal control of normal and of pathologic growths are identical. Greulich and Burford report three cases of testicular tumors in cryptorchid dogs associated with prostatic metaplasia, mammary and other sex changes. In this connection it would be interesting to know if hypertrophy of the prostate ever occurs in old untreated cases of bilateral cryptorchidism. There is no series mentioning this in the available literature. Braasch states that in cryptorchidism there is rarely an accompanying enlargement of the prostate gland.

#### EFFECT OF THEELIN ON THE PROSTATE

The injection of theelin into animals causes metaplasia and keratinization of the epithelium of the utricle of the prostate, enlargement of the prostate due to increase of the stroma, and increase in size of seminal vesicles (Moore and Price, De Jongh, Zuckerman and Parkes, and MacCallum). These effects can be neutralized by the injection of the male sex hormones (Wells, Zuckerman and Parkes, and De Jongh). The urine of normal men contains theelin (or a theelin-like substance) and male hormones; however, the variations in the amounts of these two substances in the urine under normal and pathologic conditions is but little known. Improper balance between the male and female sex hormones has been the basis for one theory of prostatic hypertrophy

(Laqueur), as well as a possible explanation for the etiology of prostatic cancer. This latter statement gets some support from our knowledge of the effect of ovarian hormone on breast tumors.

#### SOURCES OF THE MALE AND PITUITARY HORMONES: HISTOLOGIC EVIDENCE

1. *Male Hormones*.—The Leydig cells of the testis are considered to be the source of the male hormone. This inference is made from observations on the cryptorchid testis, the testis treated by x-ray, and atrophic and hypertrophied testis. In the undescended testis the seminiferous tubules are atrophic, the Sertoli cells are distended with fat, while the cells of Leydig are normal or hypertrophied. The secondary sex characteristics develop normally in most bilateral cryptorchids. Similarly in the testis treated by x-ray therapy, the Sertoli cells and interstitial cells of Leydig remain normal, although the Sertoli cells may be fat-laden. Hanes found the Sertoli cells to be constantly present in the atrophic testis and could not be sure whether they or the Leydig cells were the hormone-producing cells. However, since compensatory hypertrophy occurs in the Leydig cells when one testis has been removed and not in the Sertoli cells, he believed that the Leydig cells probably produce the secretion. Since both types of cells are usually present under most pathologic conditions, the exact rôle of each has not been ascertained (Oslund). It is possible that both have an internal secretion.

McCullagh believes that the male sex hormone, androsten, is comparable to theelin, but MacCallum believes that the watery extract of the germinal epithelium, inhibin, is more analogous to theelin, since androsten cannot cut short the excessive secretion of the hypophysis. MacCallum makes a further interesting suggestion: while inhibin restores the hypophysis to quiescence or stops or diminishes the production of gametokinetic hormone, it seems that this quiescence must also stop a second and different gonadotropic hormone which, like that which stirs the formation of the corpus luteum in the female with the production of progesterin, stirs the interstitial cells of the testis to produce lipid-soluble male hormone causing hypertrophy of the prostate. It seems important to recognize such a second gonadotropic hormone in the male comparable to the luteinizing gonadotropic of the female and to note evidences of its formation in the cells of the hypophysis in cases of prostatic hypertrophy (MacCallum).

2. *Pituitary Hormones*.—One gonad-stimulating hormone seems to come from the basophilic cells of the hypophysis. In castrates or cryptorchids these cells increase in number, swell, and become vacuolated. These changes can be reversed by the injection of theelin, watery extracts of the testis, but not by the male sex hormone or synthetic testicular hormone (Martins and Rocha, Nelson, McCullagh, and Leonard and Hisaw). The exact origin of the second gonadotropic hormone from the hypophysis is not clear. The large, slightly eosinophilic preg-

nancy cells of Erdheim and Stumme have been suggested as the source, as these cells appear during the time progesterin is liberated (MacCallum). Whether there are cells in the hypophysis of the male resembling those in pregnant females is unknown. The recent work of Evans and others describing a third gonadotropic hormone which stimulates the Leydig cells of the testis increases the field of speculation. Certainly our knowledge of the physiology of the pituitary hormones is greater than that of their anatomic sources.

#### THEORIES OF ETIOLOGY OF PROSTATIC HYPERTROPHY ON HORMONAL BASIS

From their experimental work, Lower, Engel, and McCullagh postulated a theory for the cause of prostatic hypertrophy. They believed that the gonadotropic hormone of the anterior lobe of the pituitary gland would overstimulate the secretion of androsten unless held in check; normally the spermatogenic cells are supposed to secrete enough inhibin to prevent excessive secretion of the pituitary hormone. With degenerative changes or decreased function of the spermatogenic cells, as in old age, there would be a supposed reduction in the amount of inhibin to such a degree that the functional activity of the pituitary gland would be unrestricted. As a result, excessive male hormone would be secreted and prostatic hyperplasia would develop. The Cleveland clinicians cited a series of seventy-six cases of prostatic hypertrophy which were treated by the oral administration of desiccated testicular substance; 63.1 per cent of these patients were subjectively improved. In none was there any demonstrable change in the size of the prostate. It will be noted that it was the whole testicular substance and not the water-soluble fraction (inhibin) which was used in this study.

While the above hypothesis is novel and provocative of thought, it has been criticized in that: (1) conclusions were drawn from the results of too few animal experiments; (2) impure substances were used; and (3) the histologic evidence is unconvincing in regard to the relative functional capacity of the interstitial and tubular tissues of the testis in prostatic hypertrophy. Teems found that not infrequently a good state of preservation of the seminiferous tubules and spermatogenesis is encountered between the ages of forty and eighty-nine years. Also, he found that there is a steady decrease in the number of interstitial cells in the later decades of life. Braasch believes that the absence of any convincing morphologic evidence of increased function of the interstitial cells or diminished function in the tubules during the period of prostatic hypertrophy gives only negative evidence as to their functional capacity in the secretion of autacoids.

It would be difficult to try to explain by the above theory the absence of hypertrophy of the prostate in cases of cryptorchidism or those in which the testes are injured by x-ray therapy. In such cases there is a lack or diminution in the amount of germinal epithelium and a relative

increase in the amount of interstitial tissue, which should be an ideal combination for hypertrophy of the prostate according to Lower, Engel, and McCullagh's hypothesis.

Contrary to the above view, Laqueur believes that in prostatic hypertrophy there is an improper balance between the male and estrogenic hormones, hence the abnormal changes leading to prostatic hypertrophy. Laqueur reported improvement in two-thirds of 133 cases of prostatic enlargement treated by male hormone therapy. As Koch points out, however, there have been so few studies on the rate of secretion of male and estrogenic hormones in the normal male, much less in cases of prostatic hypertrophy, that the whole subject should be considered in the experimental stage until more conclusive evidence is obtained. Hamilton, Heslin, and Gilbert found that in a series of nine men with a slight amount of residual urine, nocturia, and other sequelae induced by prostatic hypertrophy, there was no intensification of the symptoms upon prolonged treatment with estrogenic substances (500 to 1,500 I.U. theelin in oil over a period of twenty-six days). Furthermore the good results in the treatment of hypertrophy of the prostate by the administration of male hormones are hard to explain unless one postulates some anti-male hormone effect to be present, since male hormones, at least the lipid-soluble fraction of the testes, cause hypertrophy of the prostate in experimental animals.

#### INDIRECT SURGICAL PROCEDURES IN THE TREATMENT OF PROSTATIC HYPERTROPHY

1. *Castration*.—White in 1893 found that in castrated dogs there was uniformly atrophy of the glandular and then of the muscular elements of the prostate. Of 111 clinical cases of prostatic hypertrophy treated by castration, there was a high percentage (87 per cent) showing symptomatic improvement as well as clinical and histologic reduction in size of the prostate. However, castration is such drastic treatment that it is doubtful if many patients would submit to such a procedure, even if it were of proved value in the treatment of prostatic hypertrophy. Moreover, Deming, Jenkins, and van Wagenen found that in rats and monkeys the submucosal glands in the former and the mucosa of the posterior urethra in the latter were not affected by castration. They believe that there is no histologic evidence that the action produced by castration influences the growth of prostatic hypertrophy.

2. *Vasoligation*.—Theoretically one would expect little result on the prostate from vasoligation as histologically there is little change in the testes by such a procedure (Moore). Morson says that clinically division of the vas deferens per se has no effect on the size or function of the prostate. In his review Wolfson found that vasectomy alone was worthless in reducing the size of the enlarged prostate. Hada and Gotzl found no change in the dog's prostate after tying or cutting the



vas deferens. There is no large series reported in the available literature where vasoligation alone has been used in the treatment of prostatic hypertrophy. It is usually used as a prophylactic procedure against epididymitis when surgery of the prostate is contemplated. It would be interesting to examine the prostates of a large series of men who had had vasoligation years before for other reasons and compare the size of the gland with that of a group of normal men in the same age group.

3. *X-ray Therapy to Testis*.—Lower and Johnson from studies on the effect of deep x-ray therapy directed on the testes of dogs suggested that this may be of some value in reducing the size of the prostate. However, MacCallum quotes several authors who find that the secondary sex organs are unchanged after x-ray injury to the testis. 'Since the germinal epithelium is destroyed by x-ray therapy and the interstitial cells remain intact, one would expect, theoretically at least, that irradiation of the testis would be of little value in reducing the size of the prostate. Observations of such patients over a long period of years would be necessary, however, to judge the end-result and the efficacy of this treatment. Recently Geschickter has reported that in the monkey prostatic hypertrophy, which can be produced by the injection of anterior pituitary-like hormone, can be inhibited by irradiation of the testis.

#### THERAPEUTIC APPROACHES TO THE HORMONAL TREATMENT OF PROSTATIC HYPERTROPHY

It is in the case of prostatic hypertrophy with little urinary frequency, occasional nocturia, low urinary residual in the bladder, and normal kidney function that endocrine therapy might do good, especially in a prophylactic sense. The production of experimental cryptorchidism in such patients by elevating the testis to the inguinal region or instead of ligating the vas deferens, the ligation of the vessels of the cord to cause testicular atrophy might be of value to attain this end. The end-results of x-ray therapy to the testis and vasoligation on prostatic hypertrophy need further clinical investigation. However, the difficulty of getting patients to submit to these procedures and the poor economy of such measures would make hormone therapy more feasible and desirable.

According to our present knowledge, theoretically, suppression of the male hormone or the anterior pituitary gonad-stimulating substance should tend to prevent enlargement of the prostate. Whether this theory is correct or how to apply it in the clinical care of prostatic hypertrophy awaits further investigation.

It must be remembered in evaluating the results of treatment in prostatic hypertrophy that 50 per cent of men who develop prostatic enlargement never have obstructive symptoms and in a number who do the trouble is temporary (Hinman). Also, the psychic effects of any ther-

apy would have to be evaluated. The presence of infection, adenoma, or carcinoma in the prostate would add factors to complicate treatment, especially hormonal therapy. Since hypertrophy of the prostate takes years to develop, one should observe and probably treat the patient over a number of years before drawing conclusions. Certainly further data regarding the exact interrelation of the sex hormones will be necessary before a rational plan of treatment can be formulated. While one's enthusiasm must be tempered by skepticism, the day is possibly not far distant when hormonal therapy will supplant surgery in certain cases of prostatic hypertrophy.

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# Review of Recent Meetings

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## REPORT OF THE PROCEEDINGS OF THE SURGICAL CONGRESS AT GOTHENBURG, JUNE 28-30, 1937

CARL SEMB, M.D., AND JOHAN STANG, M.D., OSLO, NORWAY

**N**ORDISK Kirurgisk Forening (Nordic Association of Surgeons) held its twenty-first meeting at Gothenburg from June 28 to 30, 1937, with Professor Sven Johansson presiding.

Three main topics of discussion were on the program: (1) Cancer of the rectum; (2) examination of heart and vessels in relation to operation; (3) nonspecific affections in the lumbosacral region.

1. **Thv. Eiken**, of Aalborg, Denmark, submitted material collected in Denmark for the five-year period of 1931 through 1935. It included 1,444 cases, among which there were about twice as many men as women. Five per cent were under forty years of age, and more than one-half were above sixty years of age. In more than one-half of the cases the localization of the cancer was in the ampulla.

The extirpation by the sacral route in two stages was recommended as the routine method: first, performance of an iliac colostomy; six to eight weeks later, extirpation from below by the method of the German surgeon Goetze.

**Sam. Hybbinette**, of Stockholm, Sweden, presented his personal material on 243 cases with 113 radical operations, of which nearly all were abdominoperineal and of which 90 were performed in one stage. With regard to operability, as well as to mortality, there was a great difference between the hospital clientele (65 patients) and the private clientele (48 patients). In the group first named the operability was 38.4 per cent and the mortality 27.7 per cent, and in the latter group 70.5 per cent and 8.3 per cent respectively. The private patients had consulted a physician on an average of one-half year before the other patients. The figures, therefore, illustrate the importance of the early diagnosis. In his private clientele 40.4 per cent lived for ten years or more after the operation.

He criticized the fact that the cancer statistics reckoned with freedom from recurrence from the fifth year, while frequently metastases to the liver occurred just at that time. (Of 8 deaths in the fifth year after operation, 7 were due to metastases to the liver.)

**Elis Berven**, of Stockholm, Sweden, in the symposium emphasized that the difficulty of irradiation treatment lay in the fact that about 80 per cent of rectal cancers were radioresistant and that there was such a minimal difference between the dose which had effect on the tumor and that which damaged the normal mucous membrane.

Anorectal cancer of the squamous cell type in the first instance should have radiologic treatment. In desperate cases roentgenologic treatment should be given, because it effects cessation of hemorrhage, secretion, and tenesmus.

**G. Esbersen**, of Thisted, Denmark, had 22 cases of radical operation with no deaths. He used a personal modification of the abdominoperineal operation. The first stage was made fairly extensive with resection of the greater part of the sigmoid flexure. To avoid necrosis of the rectum, the superior hemorrhoidal artery was left intact. Rectum was removed in the second stage.

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Electrocardiography was indicated in the presence of any case of arrhythmia, with the exception of the respiratory one, and it was further an indispensable link in every examination for the evaluation of the state of the heart in individuals over forty years of age.

Torben Geill and J. Foged, of Copenhagen, Denmark, had carried out electrocardiographic examinations on anesthetized patients and had found transient myocarditic changes.

E. Svensgaard, of Copenhagen, Denmark, and Eggert Møller of Hellerup, Denmark, elucidated the value of the electrocardiogram as compared with the other methods of examination carried out in 704 heart patients.

The anamnesis alone revealed:	20% of these cases
Inspection revealed further:	4% of these cases
Stethoscopy revealed further:	41% of these cases
Electrocardiography revealed further:	21% of these cases
Roentgenologic examination revealed further:	14% of these cases

H. Krieger Lassen, of Copenhagen, Denmark, in addition to electrocardiography and roentgenologic examination, had carried out preoperative vital capacity tests. He had examined 359 patients. Even if only one of the tests—electrocardiography, roentgenologic examination, or vital capacity—deviated from normal, the mortality was 4.6 per cent greater than usual.

J. Foged found that electrocardiography revealed one-third of the latent heart diseases and made the operative prognosis safer. In a series of 1,049 patients he had a mortality of 0.50 per cent with normal electrocardiogram and 6.8 per cent with pathologic electrocardiogram. He was of the opinion that with the aid of electrocardiography one had arrived at a more accurate indication and a lower post-operative mortality.

H. Brodersen, of Oslo, Norway, had examined 100 operated patients electrocardiographically. In 48 were found pathologic changes; in 52, none. In both groups the mortality was equally high.

He criticized the reviewers because of their failure to classify the electrocardiographic patients into groups. In his own material he had distinguished between: (1) considerable, (2) small, but certain, and (3) uncertain electrocardiographic changes. Of the 48 patients with pathologic electrocardiograms, 21 belonged to Group 3, and in these no complications had occurred.

Knud Nicolaysen, of Drammen, Norway, reported electrocardiographic examinations in 400 operative patients over fifty years of age, which had revealed 4 cases of heart disease not diagnosed by the clinical examination. He maintained, therefore, that it was doubtful also whether electrocardiography would assist in reducing the postoperative complications.

Johan Holst, of Oslo, Norway, in a material of 374 cases examined had found 7, possibly primary, cardiovascular deaths. In 1 case only, however, was there correlation between the clinical findings before and after the operation and the postmortem findings.

3. In the discussion on non-specific affections of the lumbosacral region, R. Ingebrigtsen had demonstrated in 20 patients (9 women and 11 men) unilateral sacralization as a cause of pain in the back. He emphasized that severe pain in patients with this lesion was always combined with contracture of the sacrospinalis muscle, as a rule scoliosis and arthrosis in the articulation between the transverse

**R. Ingebrigtsen**, of Oslo, Norway, principally recommended abdominoperineal operation in one stage. He was of the opinion that none of the postoperative deaths after one-stage operation in his cases (5 of 28) could have been avoided by operation in two or more stages. Shock by the one-stage operation he attributed to hemorrhage. If hemorrhage was avoided or if blood transfusion was given, no severe shock was seen.

**G. Petré**n, of Lund, Sweden, had performed radical operation on 134 patients with cancer of the rectum in the period 1927 to 1936. Of these, 88 were operated upon perineosacrally with a mortality of 14 per cent. Forty-six were operated upon abdominosacrally with a mortality of 46 per cent. In spite of this difference in mortality Petré recommended the combined operation, because he holds that the great immediate mortality was compensated by the very much better late results.

**P. Bull**, of Oslo, Norway, had for treatment from 1897 to 1937, 159 rectal cancer patients in all. Ninety of these were subjected to radical operation, 53 from below with a mortality of 7.3 per cent, and 35 combined with a mortality of 22.7 per cent. Thirty-one of these 35 were operated upon in two stages with a mortality of 13 per cent. The lecturer recommended the combined method in two stages; in the first stage, colostomy only.

Other statistics were reported by **Hans Bjerre**, and **Sv. Bagger**, Örebro, Sweden; **K. K. Nygaard**, Oslo, Norway; **E. Key**, Stockholm, Sweden; **Sven Johansson**, Gothenburg, Sweden; and **S. Söderlund**, Stockholm, Sweden.

The result of the majority of statistics was a considerably higher mortality by the abdominoperineal method than by the perineosacral method. A number of speakers recommended the centralization of these operations in a few hands.

2. In the discussion on the second topic **Johannes Ipsen**, of Sønderborg, Denmark, reported his investigations comprising partly the heart function, partly the peripheral vessels in operative patients.

In his reference to peripheral vessels he particularly dealt with the changes in the skin temperature. The temperature normally rose, when the anesthesia became effective, to more than 34° C. and remained constant (Group A). In certain cases there was deficient increase (Group B); or a secondary fall occurred during the anesthesia (Group C). The mortality was much higher statistically in Groups B and C than in Group A. Especially the patients who died shortly after the operation had abnormal charts. He further mentioned that the fall in the temperature of the feet could be stopped and the temperature made to rise again by intravenous injection of gum-saline solution.

**Abraham Troell**, of Stockholm, Sweden, gave an account of examinations of the heart in 287 thyreotoxic patients. In an abnormal roentgenogram of the heart and in an abnormal electrocardiogram he found that the operative mortality was increased, being three or four times as great as in normal findings.

**Eggert Møller**, of Hellerup, Denmark, as internist reviewer, stressed the fact that there was a great difference in the prognostic importance of the various diseases. Aortitis, myocarditis, and coronary sclerosis are the essential causes for operative mortality increasing with rising age.

Roentgenologic examination was the safest means of deciding whether, in a given case, an organic disease of the heart existed. This was due to the fact that the dilatation was the first compensatory step of the damaged heart.

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Carl Semb, of Oslo, Norway, discussed clinical aspects of the lumbosacral lesions, particularly the symptom of radiating pain, which was an expression of reflex neuralgia and which had great diagnostic value. In the presence of lesions of the lumbar column radiating pain occurred in the anterior part of the femur corresponding to the lumbar segments. In lower lesions, iliosacral lesions for example, radiation to the posterior side of the femur and crus was usual. The necessity for cooperation with the neurologists was emphasized.

In two cases of bilateral sacralization Semb had performed a fixation or arthrodesis between the transverse process and massa lateralis by a grafted piece of the iliac crest. The patients became symptom free.

In two cases of painful articulation between the spinous processes of the lumbosacral region he had carried out resection of the spinous processes with good results.

Nils Silfverskiöld, of Stockholm, Sweden, discussed the importance of the shape of the sacrum based on 100 skeleton studies. With regard to the treatment of the sacralization and the spondylolisthesis, he strongly recommended conservative treatment. The sequence of the therapeutic measures should be as follows: (1) ordinary régime; (2) cast and exercise therapy; (3) operation.

As a supporting bandage in these lesions, he used a plaster cast for three to six weeks, then careful exercise therapy. The great majority of patients got rid of their symptoms by this treatment. Only as ultimate refuge should operation be resorted to.

Fr. Roscher, of Arendal, Norway, reported two cases of bilateral sacralization treated with resection of the transverse processes, resulting in cure.

Hindahl, of Denmark, also stressed the fact that conservative treatment should be tried in the first instance. In the presence of unilateral sacralization he preferred to carry out a fusion operation. He used Hibbs' method of spondylolisthesis.

A number of different papers were presented, in addition to the topics of discussion mentioned in the program.

John Hellström, of Stockholm, Sweden, gave a paper on the incidence of persisting discomfort after cholecystectomy, which was based on 1,372 operated cases of cholelithiasis or cholecystitis. Follow-up examinations had been carried out in 1,041 patients, of which only 32.1 per cent were completely free of symptoms. Biliary colic persisted in 28.9 per cent, and gastrointestinal discomforts in 62.2 per cent. In women such discomforts persisted to a much greater extent than in men. Among those who had biliary colic after the operation were found 9 cases of common duct stone, necessitating another operation. Some of the gastrointestinal symptoms were explained by the achylia. The incidence of persistent discomfort was much less in patients who were operated upon after the first attack.

K. K. Nygaard, of Oslo, Norway, mentioned the postcholecystectomy syndrome and the postoperative strictures of the biliary duct. He drew attention to the investigations carried out by Walters, which demonstrated that morphine and pantopon caused a spasm in the sphincter of Oddi with resultant pain, while amyl nitrite and glyceryl-trinitrate relaxed the spasm.

Ph. Sandblom, of Örebro, Sweden, had carried out investigations regarding Montproffit's cholecystojejunostomy, and he had found that this method was inferior to the gastrocholecystostomy.

Sture Rödén, of Stockholm, Sweden, had made a number of interesting "abdominal window" studies, and with the aid of a color film demonstrated the effect

process and massa lateralis of the sacrum, and in some cases spondyloarthrosis. The presence of unilateral sacralization without symptoms was found more frequently in men than in women.

The indication for treatment should be that no other demonstrable cause of pain was present. Further, the symptoms ought to be so severe that the patient was unable to work. Resection of the transverse process then would lead to cure.

**S. A. Brofelt**, of Helsingfors, Finland, in a series of 232 cases of low back pain, in which were not included polyarthritic and ankylopoetic lesions, had 42 unilateral sacralizations, 42 spondylolistheses, 8 spondyloses, 6 posterior displacements of vertebrae, and 29 cases of horizontal sacrum.

The lecturer discussed the importance of the angle between the sacrum and the lumbar column. The 29 cases with horizontal sacrum or sacrum acutum arcuatum all had more or less lumbosacral discomfort. The cause of this could be, he considered, the strain on the iliolumbar ligament.

He attached importance to the fixation by operation, including the three lower lumbar and the two upper sacral processes. The tibial graft was given a slightly angular shape so as to fit better into the lumbosacral curve. Confinement to bed for seven to twelve weeks and encasement in a plaster cast for eight to twelve months followed.

**Sig. N. Bakke**, of Bergen, Norway, as roentgenologic reviewer, reported on a series of 1,146 patients in whom the lumbosacral joints were compared mutually; he found asymmetry in 56 per cent. He was of the opinion that this asymmetry played a decisive part, because the strain on asymmetric articulation surfaces causes trophostatic changes. By examination of unexplicable scolioses in a great number of cases were found frontally placed, oblique articulation surfaces in the lumbosacral joints on the concave side of the scoliosis.

In 1,893 patients examined, the reviewer had found 139 (7.3 per cent) with unilateral sacralization. The most frequent change in 34 patients with unilaterally joined sacralization who suffered pain was oblique position of the vertebra; also there was deformity of the lumbosacral joint and finally changes in the intervertebral disk.

He looked upon the cleft in the lateral arch as a prespondylolisthetic condition. All of the 19 spondylolisthetic cases of the reviewer had stopped their slipping spontaneously. He also mentioned some cases of pseudospondylolisthesis (slipping in spite of the lack of cleft in the lateral arch), and maintained that these conditions were also dependent upon a defect in the arch, increased lordosis, and degeneration of the corresponding intervertebral disk. Further he mentioned briefly posterior slipping of the vertebral corpus, spina bifida occulta, hemispondylus, as well as ossification and calcification of the ligamentary apparatus.

**Sten Friberg**, of Stockholm, Sweden, had used Albee and Hibbs' method for operative treatment of spondylolisthesis. In 3 cases, however, he had performed laparotomy and resection of the intervertebral disk with subsequent grafting of a piece of the iliac crest.

**R. Malmros**, of Copenhagen, Denmark, reported 7 cases of rupture of the intervertebral disk. He was of the opinion that this lesion might be traumatic, or might be caused by degeneration of the disk, or by both these factors combined.

The pain was the predominant symptom, but there occasionally also occurred myoclonus, tremor and atrophies.

Examination generally disclosed tenderness over the corresponding spinous process. Occasional elevation of the spinal fluid protein occurred. Ordinary roentgenologic examination was negative. The condition could not be diagnosed until a contrast medium was injected into the spinal canal.

Johan Holst replied to Perman. If the pleura was thin, it was not advisable to destroy the periosteum because deficient regeneration may cause expansion of the lung. Resection of the transverse processes was superfluous, and in addition it caused extensive scoliosis.

C. Semb criticized the method used by Perman in that it did not give concentric collapse and that it necessitated needlessly great rib resections with danger of paradoxical respiration.

In his cases with extrafascial apicolysis Semb had a mortality of 3 per cent and collapse of the cavity in 90 per cent.

C. Semb gave a paper on the treatment of persistent cavities after previous thoracoplasties. He advised extrafascial apicolysis with resection of ribs correspondingly and, if necessary, resection of the transverse processes around the upward attachment of the apex of the lung in the second stage. The upper periosteal beds were mobilized posteriorly to enable them to collapse together with the apex and to fix the latter in its collapsed condition by regeneration of ribs. In 19 operated cases he had 1 postoperative death. In all of them except 2 cases collapse was obtained as well as freedom from bacilli.

G. Nyström, of Uppsala, Sweden, had experienced infection of the wound cavity in 20 per cent when using apicolysis, and he asked Semb how to avoid infection.

C. Semb pointed out that the apicolysis should not be made larger than required, that badly nourished intercostal musculature over the top of the lung had to be removed. Drainage, if at all necessary, should be of brief duration (twenty-four hours). Preliminary skin treatment for acne was important. In the presence of fistulas reoperation had to be carried out with excoriation and primary closure, and in some cases resection of the clavicle.

Saved Ribbing, of Uppsala, Sweden, had found, by histologic and roentgenologic examinations of the epiphysis of the lower femur in children from three to nine years of age, free bone islets close to the outline of the epiphysis in many cases. The localization of these bone nuclei corresponded to the place of predilection for osteochondritis dissecans at an older age and was assumed to be the constitutional factor in the etiology of this lesion.

O. Aleman, of Stockholm, Sweden, recorded a series of 91 fractures of the navicular bone, of which 79 cases were cross-fractures. Twenty-four of the latter were operated upon with removal of the smallest, or distal, fragment. The results of the operations were very good in 20 cases, good in 4 cases, and bad in no cases.

C. Semb drew attention to a few details of the nailing of fractures of the neck of the femur. He had constructed his own splint with a revolving crural attachment, which made it possible to obtain an effective inward rotation of the femur. After reposition by skeletal traction on this splint, the operation could be postponed until the general condition of the patient was satisfactory. The operation was performed with the patient in bed, and traction's being continued, by the Smith-Petersen/Johansson method. A sighting apparatus of own construction was used.

Of 101 operated cases subsequent displacement occurred in 4 cases only, of which the 3 were renailed with good results. There were 2 deaths; 1 from apoplexy.

S. Johansson, of Gothenburg, Sweden, maintained that the pronation did not play such an important rôle for the reposition. He himself used Braun's splint with traction on the tibia. He had operated upon 180 patients. The mortality was 10 per cent; the percentage of cure was 90 to 95 per cent.

of the peritonitis on the peristalsis. He further demonstrated that injection of hypertonic saline solution had a better and more lasting effect than peristalsis-inciting preparations.

K. K. Nygaard gave an account of a graphical method for the determination of the coagulability of the blood according to a photo-electric principle. A transportable coagulograph constructed by the speaker was demonstrated.

Einar Ljunggren, of Sollefteå, Sweden, pointed out the similarity in the pyelogram of cystic pyelitis and of renal tuberculosis. He advised against operation on the roentgen diagnosis alone.

Hans Hellmer, of Lund, Sweden, treated the intravenous urography as a morphologic diagnostic procedure, and stressed the importance of carrying out increasing compression in order to obtain good pictures of the renal pelvis. He also recommended the use of softer rays and longer exposure to ensure that the ureters appeared clearly.

C. Crafoord, of Stockholm, Sweden, gave a paper on the diagnosis and treatment of the malignant tumors of the lung. He emphasized the importance of the roentgenologic examination—the bronchoscopy, and particularly the bronchography.

C. Semb maintained that the preliminary pneumothorax also belonged to the diagnostic facilities besides presenting advantages with a view to the subsequent operation. Semb treated in more detail three cases of intrathoracic tumors (fibroma of the lung, pericardial cyst, cancer of the lung—all removed), which had caused considerable diagnostic difficulties.

Johan Holst had operated upon 3 cases of cancer of the lung. One patient, in whom the upper lobe was removed, survived and was free from recurrence two years after the intervention.

Einar Key, of Stockholm, Sweden, mentioned 3 cases of cystic bronchial cavities, which had been confused previously with empyema. They had all been lobectomized.

Johan Holst gave a paper on lobectomy for bronchiectasis. He had performed 12 lobectomies and 1 pneumonectomy, mainly according to the technique of Brunn-Shenstone. The lesion was unilateral in 11 cases and bilateral in 1 case. Three patients had bronchiectatic cavities nearly the size of hen's eggs. All patients with unilateral lesion recovered—8 were symptomless; 2 are still under treatment.

E. Perman, of Stockholm, Sweden, gave an account of his thoracoplasties. He used a method of operation similar to that of Alexander-Maurer—large curved incision round the scapula. The arm on the diseased side was flexed alongside the head so as to obtain a less exposed position of the vascular and nerve plexus. Large pieces of the ribs were resected, particularly of the fourth and fifth ribs, with resection of the transverse processes. There was no apicolysis. The scapula was tipped under the ribs so as to be of service in the compression. He used painting with a solution of 4 per cent formalin in order to prevent regeneration of the periosteum. He had operated upon 40 patients with 2 deaths. All were operated upon in two stages.

Sven Lundberg, of Gothenburg, Sweden, performed his thoracoplasties under avertin anesthesia, in two stages: in the first stage anterior incision in the thorax with resection and apicolysis; three weeks later paravertebral resection from below upwards. The three upper ribs were totally removed. He spoke against resection of the transverse processes.

by inhalation, because he feels that in not a few cases it causes a rise in temperature which is not attributable to some form of disease. The oral method of intubation for intratracheal anesthesia is preferred to the nasal method, because it is felt that in the nasal method there may be unnecessary trauma to the turbinates.

Dr. H. J. Shields, of Toronto, uses nupercaine for spinal anesthesia for upper abdominal surgical operations, employing the Howard Jones technique. He uses procaine in doses of from 250 to 300 mg. for thoracic operations. The total dose of procaine is dissolved in 10 to 12 c.c. of spinal fluid. Intravenous infusion is maintained throughout the course of the operation in order to combat any sudden fall in blood pressure. Dr. Shields has suggested that 50 c.c. of distilled water be injected intravenously in cases of headache following spinal anesthesia or in cases of any headache resulting from lumbar puncture. Why this procedure seems to be effective is not thoroughly understood.

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## REPORT OF THE MEETING OF THE FIFTH INTERNATIONAL CONGRESS OF RADIOLOGY IN CHICAGO, ILL., SEPT. 13-17, 1937

LEO G. RIGLER, M.D., MINNEAPOLIS, MINN.

*(From the Department of Radiology of the University of Minnesota)*

THE fifth congress of radiology of international scope was held in Chicago. The difficulty of summarizing the proceedings of a meeting which was held in nine sections and during which well over 200 papers were delivered in at least five languages can readily be imagined. The session was extraordinary both in its size and scope, and in the quality of the papers and exhibits. Only a few of the more important matters of general interest can be reported here.

The Use of the Roentgen Rays in the Diagnosis and Treatment of Tumors of the Bladder was presented by George E. Pfahler, of Philadelphia, Pa. He detailed his method of pneumocystography as a supplement to cystoscopy. Roentgen study after air injection permits better determination of the degree of infiltration of the bladder wall, the differentiation of papillomatous from infiltrating forms of carcinoma. Pfahler advocates roentgen therapy for inoperable tumors, reporting occasional startling cures. Combined intravesical destruction and irradiation is important. Cures of two to five years' duration were reported in 50 per cent of all the cases.

Gösta Forssell, of Stockholm, summarized his noteworthy researches on The Role of the Autonomous Movements of the Gastrointestinal Mucous Membrane in Digestion. He has demonstrated that the mucous membrane of the entire gastrointestinal tract moves independently of the muscle wall. He emphasized particularly that in this way recesses are created which are of vital importance in the digestive processes.

Carl Sandström, of Stockholm, described the Diagnosis, Pathology, and Roentgen Treatment of Peritendinitis Calcarea, usually called calcifying bursitis in this country. He reported cases of this type not only in the shoulder but also about practically all the joints of the extremities. Studies of the pathology show clearly that the calcification is secondary to necrotic changes in the tendons,

S. Johansson also demonstrated 3 patients. In the 1, who had lost a thumb, he had prepared a new one by transplanting a tibial graft in the metacarpal bone and surrounding this with skin graft. The result was remarkably good.

E. Platon, of Oslo, Norway, gave a film demonstration of an extreme case of *recurvatio genu congenitum*, which made a four-legged creature of the patient. The operation here gave an excellent result with an erect walk.

## MEETING OF THE ANESTHETISTS' TRAVEL CLUB, MONTREAL AND TORONTO, OCT. 18-23, 1937

EDWARD B. TUOHY, M.D., ROCHESTER, MINN.

*(From the Mayo Clinic)*

A MEETING of the Anesthetists' Travel Club was held in Montreal and Toronto; three days were spent in each city. Dr. Wesley Bourne, Dr. C. C. Stewart, and Dr. Harold Griffith were the hosts in Montreal and they demonstrated the methods of anesthesia which they currently use. The intratracheal method of general anesthesia, with cyclopropane as the anesthetic agent, is used predominantly. For certain types of operations, especially lower abdominal work, basal dosages of tribromethylalcohol (avertin) are used in conjunction with intratracheal administration of cyclopropane and oxygen.

The agent which is most commonly used for spinal anesthesia is nupercaine; a 1:1500 solution is employed, either by the Etherington-Wilson or the Howard Jones technique.

In the former method the patient is in the sitting position while the lumbar puncture is being made; and after the contemplated dose of the solution of nupercaine has been calculated, it is injected and the patient is maintained in the sitting position for a limited time, usually from fifteen to forty-five seconds, before being placed horizontally on the table. The Howard Jones method consists in performing spinal puncture, preferably with the patient lying on his side, and the height to which anesthesia is to progress is regulated by tipping the table so that the patient is held in varying degrees of the reverse Trendelenburg position. The doses of solution of nupercaine used in this technic, and in the Etherington-Wilson technic, are calculated on the same basis, the usual amount varying from 9 to 15 c.c.

Dr. Griffith uses cyclopropane for intratracheal anesthesia in operations on the eye, ear, nose and throat of children; he employs a silk woven catheter covered with rubber. The usual size of the catheters used in work with children varies from 24 to 30 French.

In connection with one of the obstetric departments in Montreal, it is the practice to collect blood from the placenta at the time of delivery. This blood is put in sterile containers, using sodium citrate as the anticoagulant. It is possible to obtain between 150 and 300 c.c. of blood in this manner and after the blood has been grouped it can be used for transfusions as is seen fit. It is noteworthy that the blood obtained from the placenta contains a great number of red blood corpuscles, frequently 7,000,000 per cubic centimeter. The method of keeping blood in the ice box for a limited time, not more than three weeks, also is used.

Dr. C. H. Robson, of Toronto, is employing intratracheal cyclopropane anesthesia with children, using the woven silk catheter previously mentioned. He is of the opinion that atropine should not be administered to children prior to anesthesia

he was able to demonstrate small stones which were invisible in the ordinary cholecystograms. The position of the stones in relation to the gallbladder dye depends upon their specific gravity as compared to that of the bile and dye mixture. In some cases the stones form a layer of lessened density at the very tip of the fundus; in other cases they layer themselves in the middle or near the superior pole of the gallbladder. A similar study was presented by Arnold Bernstein, of Danzig. He emphasized particularly the demonstration of calcium bile in this same manner.

**Adaptability of the Mediastinum to Various Physiological and Pathological Conditions** was discussed by John Alexander and C. B. Peirce, of Ann Arbor, Mich. They described the changes in position and shape of the mediastinal structures which follow various normal and pathologic changes in the thorax.

**Cerebral Cystography and Cisternography** was presented by Arthur Schueller, of Vienna. He described in detail the roentgen findings in a variety of intracranial cysts, including the evidence derived from ventriculography with direct filling of the cysts with air. He also discussed the encephalographic demonstration of the changes in the cisternae of the brain which occur from various diseases. Schueller also advocated the intraspinal injection of iodized oil and the filling of the cisternae with the contrast medium by inversion of the patient.

**The Value of Encephalographic Studies Following Head Injuries** was presented by J. T. Travers of New York, N. Y. He described particularly cases of subdural hematoma, intracerebral hemorrhage, and brain atrophy, in which encephalography done three weeks or more after the injury clarified the nature of the intracranial lesion.

**W. J. Mixter**, of Boston, Mass., discussed **Rupture of the Intravertebral Disk** reviewing our present knowledge of this subject and detailing again the diagnostic criteria which have been described in previous papers. **Harry A. Olin**, of Chicago, Ill., described the general involvements of the intervertebral disk from injury or disease. He believes the disk may be readily injured by spinal puncture. Olin found extrusion of the nucleus pulposus into the vertebral body in 84 per cent of 50 cases of fracture of the spine.

**Hans H. Berg**, of Hamburg, presented his observations on **Gas Filling of the Bile Ducts**. He described numerous cases in which gas was demonstrated at the internal duct system by roentgen examination. In one group this was due to biliary fistula from a variety of causes, chiefly the erosion of a gallstone. In the second group the gas resulted from infections of the biliary tract, cholangitis with and without abscess. Berg believes that more careful roentgen examination of the liver region in cases of undiagnosed abdominal conditions or complicated hepatic or gallbladder diseases will reveal many more of these cases and thus afford a clue to the nature of the lesion.

**J. A. Saralegui**, of Buenos Aires, detailed some more recent observations on **Cholangiography**. He advocated a simple surgical procedure as a first stage operation in diseases of the gallbladder and biliary system; i.e., the insertion of a drainage tube into the fundus of the gallbladder. A week or so following, thorium dioxide sol (thorotrast 50 per cent) is injected and roentgen studies are made. Depending upon the roentgen findings, further surgical procedures of a more radical nature may be undertaken. By means of cholangiography he is able to demonstrate practically all of the normal and abnormal conditions which affect the biliary duct system and the gallbladder.



peritendinous connective tissue, periosteum, joint capsules, and ligaments. Roentgen ray treatment is highly effective, resulting both in the relief of symptoms and the disappearance of the calcium shadows.

A summary of the rôle of roentgenkymography in diagnosis was presented by Pleikart Stumpf, of Munich, the originator of this method. Kymography has two purposes: the fixation for study of movements which can also be observed more fleetingly in the fluoroscope; the observation of movements which occur so rapidly that they are not clearly seen on fluoroscopy, or so slowly that they are not noticed at all. He described his studies on the movements of the heart, lungs, thyroid gland enlargements, the gastrointestinal tract, and the upper urinary tract.

Motion pictures made from the image on the fluoroscopic screen were demonstrated by Russell J. Reynolds, of London, a pioneer in this field. He showed very effectively, in this way, the motions of swallowing, pulsations of the heart, movements of the diaphragms, lungs, and mediastinum. This method of demonstrating the movements of the stomach is much less effective under present technical conditions because of the short period during which the exposures may be made.

One of the most outstanding events of the Congress was a motion picture demonstration of the physiology of the heart in animals presented by Werner Boehme, of Rostock, Germany. Boehme first injects the animal with sufficient thorotrast to make the entire cardiovascular system, especially the cardiac chambers, brilliantly visible on fluoroscopy. Following this a second injection of iodized oil is made into the vein. Motion pictures at exceedingly great speeds then are made of the fluoroscopic image. The individual chambers of the heart can be seen and the droplets of oil are observed passing along the larger veins to enter the heart. In this manner many of the problems of cardiac physiology may be studied without opening the thorax or injuring the cardiovascular system.

Nils Westermark, of Stockholm, presented a very illuminating paper on *Bronchial Carcinoma, A Roentgen-Pathological Study*. He described the roentgen findings of very early carcinoma of the bronchus as a slight degree of localized atelectasis followed shortly by a more extensive area of emphysema. Repeated examinations will show increasing atelectasis following which bronchography will usually reveal a stenosed bronchus. From his studies Westermark believes the majority of bronchial carcinomas to originate in the smaller bronchi and to extend centrally at a later date. For this reason bronchoscopy may be ineffective as a diagnostic measure in the very early stages of the tumor.

*The Malignant Bronchial Stenosis, Bronchographic Aspect* presented by Pedro L. Farinas, of Havana, Cuba, described his studies using serial bronchography in the diagnosis of carcinoma of the bronchus. He attempts to distinguish between benign and malignant tumors of the bronchus and between the various types of malignant lesions by the character of the filling defect shown in the bronchogram. It is often difficult, however, to distinguish a tuberculous stenosis from a malignant one. The method is of particular value in the diagnosis of tumors of the smaller bronchi in which bronchoscopy is of little value.

Ake Akerlund, of Stockholm, presented a review of his work on *Layer Formation in Vertical Cholecystography as an Aid in the Diagnosis of Small Gallstones*. He described the varying densities of gallbladder bile which cause a layering of the contrast medium when films are made with the patient standing. By making exposures during fluoroscopic observation, with pressure, in the upright position,

he was able to demonstrate small stones which were invisible in the ordinary cholecystograms. The position of the stones in relation to the gallbladder dye depends upon their specific gravity as compared to that of the bile and dye mixture. In some cases the stones form a layer of lessened density at the very tip of the fundus; in other cases they layer themselves in the middle or near the superior pole of the gallbladder. A similar study was presented by **Arnold Bernstein**, of Danzig. He emphasized particularly the demonstration of calcium bile in this same manner.

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B. R. Young and Michael Scott, of Philadelphia, Pa., described the use of air as a contrast medium in the roentgen examination of the spinal cord. While not as accurate as iodized oil, it may be helpful in many cases and it does not have the deleterious effects attributed to the oil.

The general subjects of epiphyseolysis or separation of the proximal femoral epiphysis and aseptic necrosis of this epiphysis were discussed by R. Pomeranz, of New York, N. Y., and A. Herzog, of Czechoslovakia. The former described the findings in various stages based on 180 cases of slipped femoral epiphysis. He indicated the varying end-results of this lesion. Herzog related aseptic necrosis of the femoral neck to epiphyseolysis. He emphasized the points of distinction between aseptic necrosis, tuberculosis, and pyogenic infections and brought out that aseptic necrosis of the neck may follow a slipping of the epiphysis.

Carl Wegelius, of Helsingfors, presented data to show that urine is reabsorbed, probably from the kidney pelvis. By roentgenographic means, he made volumetric determinations of the quantity of urine in the bladder. It appears that healthy individuals, whose bladders were greatly distended from drinking water, showed a recession in several hours of as much as 60 to 90 c.c. in the volume of the bladder without micturition.

Numerous papers were presented by a number of investigators on the relatively new procedure of tomography or planigraphy or laminagraphy, all of which detailed the uses of this method of roentgen examination in a variety of conditions. Essentially these procedures involve the production of roentgenograms which exhibit the structures in certain planes of the body with sharp detail while blurring out all the structures in all other planes. With a rather complex apparatus, in special instances, considerable improvement in roentgen diagnosis can be obtained. This is particularly true of such deep-seated structures as the sphenoid sinuses or in extensive disease of the lung. By the use of "subtraction" as described by Zeides Des Plantes, of Utrecht, a similar result is obtained by a different method. The complexity of the procedure, together with the necessity for using numerous films, has militated against the general acceptance of the method.

Albert Oppenheimer, of Beirut, discussed **Acute Transient Intestinal Atony**, emphasizing the distention of the colon and even of the small bowel occurring during pyelography and renal colic. He believes this is due to inhibitory nervous impulses. It may occur as an independent transient phenomenon, accompanied by severe colicky pains, spontaneously subsiding in a few days. Most commonly it is secondary to other lesions such as duodenal ulcer, biliary colic, mesenteric thrombosis, etc.

Philipp Sayhoun and Albert Oppenheimer also presented new material on the roentgen diagnosis of appendicitis. They found stasis in the appendix to be due to degenerative changes in nerve ganglia with impairment of the peristaltic activity of the appendix. With these changes there usually occurs a leucocytic infiltration, probably inflammatory. A peculiar roentgen appearance, in the form of semilunar filling defects, may indicate an inflammatory edema of the mucosa, an acute phase of the appendiceal stasis.

The Janeway Lecture of the American Radium Society was delivered by Douglas Quick, of New York, N. Y., on **Carcinoma of the Larynx**. He reviewed the history of the treatment of this disease. He has abandoned the terms intrinsic and extrinsic, but substitutes for them carcinoma of the larynx proper

(intrinsic) and carcinoma of the hypopharynx (extrinsic). Quick believes that the results achieved with high voltage x-rays during the past five years make total laryngectomy an obsolete procedure. The most important features of the application of radiation therapy are daringly intensive radiation and individualization of the case.

Henri Coutard, of Paris, also presented the results of roentgentherapy of cancer of the larynx after five and ten years of observation. The differences in results are much more dependent on the histologic type than on the extent of the lesion. Those of the cutaneous type, which are highly differentiated and most infiltrative, are least responsive, while the epitheliomas of the mucous membrane type are most readily cured. In the latter, various types of treatment have been successful. In the former, changes in methods of treatment have been of little avail. Coutard reported 27 per cent of all his cases treated from 1921 to 1932 cured for a five-year period. The cures have been maintained, on the whole, for a ten-year period.

Hans Holfelder, of Frankfort, presented a method for evaluating the results of radiation therapy. In general, he reviewed the information such as the nature of the tumor, the quality and quantity of the irradiation, the method of application, etc., and suggested exact methods for recording these data.

Hermann Holthusen, of Hamburg, reviewed his own well-known work on the relationship of the biologic nature of tissues to their reaction to irradiation.

The League of Nations' Work on Uniform Statistical Presentation of Results in Radiotherapy of Uterine Cancer was presented by James Heyman, of Stockholm. The report of this committee concerned itself with a proper anatomic classification of cases, with recommendations for proper statistical methods and with procedures for calculating results.

Fred Taussig, of St. Louis, advised the use of iliac lymphadenectomy together with irradiation in the treatment of cervical cancer. He reported improved results with this method.

Auguste Gunsett, of Strasbourg, reported his experiments with the use of 520 kv. as compared to 200 kv. x-rays. He is firmly convinced of the superiority of the higher voltages. S. G. Mudd, C. K. Emery, and L. M. Levi, of Pasadena, Calif., also reported more encouraging results in the treatment of various cancers when supervoltage x-rays were employed. R. S. Stone, of San Francisco, Calif., discussed his experiments which appear to demonstrate that skin reactions were not less with 1000 kv. x-rays than with 200 kv. x-rays. From the standpoint of skin tolerance, super voltage is only of advantage in extremely thick parts or when cross-fire is not used. T. Leucutia, of Detroit, Mich., reporting on a comparison of clinical results over a three-year period using 500 kv. and 200 kv. therapy, found that the higher voltages were superior only in those cases in which the carcinoma is very deep seated or has infiltrated surrounding tissues to a considerable degree. The outstanding example of this improved response is in the frozen pelvis due to carcinomatous infiltration from carcinoma of the uterine cervix.

Further evidence favoring the fractional method of irradiation was brought out by Carl Fried, of Breslau. He emphasized the use of this method particularly in inoperable tumors and reported surprisingly good results in certain cases of gastric cancer, brain tumors, and advanced carcinoma of the breast and bladder.

Wm. E. Howes, of Brooklyn, N. Y., and G. T. Pack and Gordon McNeer, of New York, N. Y., likewise recommend greater use of radiation therapy in the inoperable cases of carcinoma of the stomach.

Alexander Brunschwig, of Chicago, Ill., reported his observations on the histology at the site of benign giant cell tumors several years after conservative treatment, such as irradiation or curettage. There is an unusual slowness of reossification in such tumors so that roentgenograms several years after treatment may show little change from the original appearance in spite of the fact that no tumor remains.

Congo Red and Liver Therapy in Roentgen Sickness was discussed by Isidore Arons and Boris Sokoloff, of New York, N. Y. They found that Congo red and liver combined were of practical value in combating both the roentgen sickness and the anemia which often follow irradiation. Incidentally, they discovered that these two substances, in themselves, exercised a pronounced inhibiting effect on the growth of mouse sarcoma.

An extensive symposium on the radiation therapy of carcinoma of the breast was held, some eight papers being presented. The essayists discussed various phases of this problem, but there was general agreement that a combination of surgery and irradiation is the best method of treatment. Good results were reported with the use of preoperative as well as postoperative irradiation. Simple mastectomy with postoperative x-ray therapy, in one series of cases, seemed to afford a relatively high percentage of cures.

An important review of irradiation therapy of cancer was given by Hans R. Schinz, of Zurich, who reported his observations over a seventeen-year period.

The treatment of acute pneumonia, particularly of the lobar type, by x-radiation was reported on by Eugene Powell of Temple, Tex., and Carl Fried, of Breslau. The latter presented experimental evidence to support the clinical experience of the rapid resolution of both lobar and postoperative pneumonia. M. Berck, of New York, N. Y., again reviewed the results of roentgen therapy for bronchiectasis. He believes that moderately large doses of x-rays present a feasible and successful treatment for many cases of chronic secreting bronchiectasis.

Most of the papers presented in the sections on radiobiology and radiation physics were of a highly technical nature. There were a number of presentations detailing investigations on the effects of neutrons on biologic materials.

John H. Laurence, Paul C. Aebersold, and Raymond E. Zirkle, of Berkeley, Calif., reported the varying effects of neutrons on different substances leading to the possibility that this form of radiation may be specifically more effective than radium or x-rays on certain neoplasms.

J. Gershon-Cohen, Harry Shay, David R. Meranze, and Samuel S. Fels, of Philadelphia, Pa., reported their observations on the irradiation of the thymus in rats. The atrophy produced seemed to have a definite relationship to general growth, skeletal development, and particularly to development of the genital system.

Numerous other papers of great interest to the radiologist and the physicist, but of less general interest, were presented.

# Book Reviews

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**Operative Surgery, the Ear, Air Passages and Neck.** By Dr. Martin Kirschner (with the collaboration of A. Lautenschläger and O. Kleinschmidt). Authorized translation by I. S. Ravdin and George M. Coates. Pp. 528, with 460 illustrations. Philadelphia and London, 1937, J. B. Lippincott Company. \$10.

This, the third volume in the operative surgery series of Professor Martin Kirschner, of Heidelberg, is worthy of the distinction of appearing on the shelf beside its two illustrious predecessors. This volume appears in two parts; the first relates to operations on the ear, the nose and its appendages, the pharynx, larynx, trachea, and bronchi. This section is written by Professor Lautenschläger, of Berlin, and is edited and translated by Dr. George M. Coates, of Philadelphia. Part Two concerns operations on the esophagus and other structures of the neck and is written by Professor Kleinschmidt, of Wiesbaden, and is edited and translated by Dr. I. S. Ravdin, of Philadelphia, who also sponsored the appearance of the first two volumes in English.

The approach to the description of operative procedures is distinctly anatomic. The influence of years of contact with cadaver surgery in the teaching of applied surgical anatomy to medical students, an exercise to which every academic German surgeon is thoroughly exposed, is immediately apparent. The anatomic plan of operation so well elucidated by the authors is worthy of careful study. Physiologic considerations relating to the operations described, however, are often totally ignored by the writers. In the section on the neck, some of the obvious omissions have been repaired in part by the insertion of short pertinent sentences by the editor.

The illustrations, of which there are a large number, are beautifully done in color and add much to the effectiveness of the descriptions. How often American authors have occasion to be envious of their continental colleagues whose publishers permit them to use illustrations in color so generously.

A serious omission, the reviewer feels, is failure to append a satisfactory bibliography. Scores of names (largely German) are cited throughout the volume, but where these references are to be found is not intimated. The usefulness of the volume would have been increased several fold to the critical student of surgery by the proper insertion of suitable references.

The volume can be whole-heartedly recommended to any serious student of surgery having an interest in the subject matter.

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**Surgical Treatment.** By James Peter Warbasse and Calvin Mason Smyth, Jr. Third vol. Ed. 2. Pp. 906, vol. I; 782, vol. II; 798, vol. III. Philadelphia, 1937, W. B. Saunders Company. \$35.

Francis Bacon, in his day, took all knowledge for his province. With the development of science—which Oliver Wendell Holmes defined as the topography of ignorance—men have become less bold in their excursions into diverse branches of learning. No man longer essays to encompass the entire field of medical knowledge. Surgery, too, has become so broad that no one man's or even two men's knowledge extends completely into its numerous ramifications. In this weakness lies the fundamental defect of these volumes.

Jacobsen and Kocher, profound students of surgery in their day, were able to write, unaided, works on operative surgery which their contemporaries and even men of our generation have zealously studied. Jacobsen's *Operations of Surgery* and Kocher's *Operative Surgery* became the *vade mecum* of Anglo-Saxon and Teutonic surgeons. The authors of those volumes directed their efforts to help instruct the best informed surgeons. In consequence, they fathered texts which reached an unusually large audience.

The authors of these three volumes on surgical treatment have essayed to discuss both nonoperative and operative treatment of surgical disorders. They have levelled their effort undoubtedly at the general practitioner who will find contained in these volumes a surprising mass of useful information. The experienced surgeon will find in them much to commend and much with which he will disagree or which he will feel inclined to criticize. He will miss particularly the critical scholarly attitude which he is wont to expect in a work of this magnitude. He will note the absence of references—a serious omission in the eyes of the inquisitive and fact-seeking surgeon. He will find statements once contained in texts that are now obsolescent. It is to be hoped that when a third edition of these volumes is written many of its inaccuracies will be corrected by the inclusion of more authors whose fused efforts will constitute a more scientific and authoritative treatise. The wide audience of American surgeons is deserving of the best conjoint effort of a strong medical publishing house and alert and experienced surgeons possessed of a scientific and scholarly interest. Volumes which are sufficiently authoritative to instruct the best informed of surgeons are also the most valuable and the safest sources of information for the "occasional surgeon."

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**Synopsis of Digestive Diseases.** By John L. Kantor. Pp. 206, with 40 illustrations. St. Louis, 1937, The C. V. Mosby Company. \$3.50.

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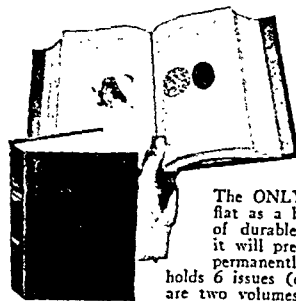
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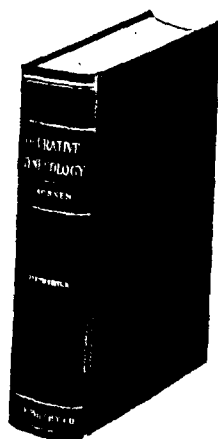
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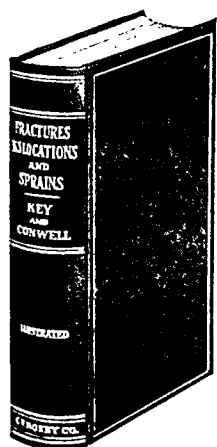
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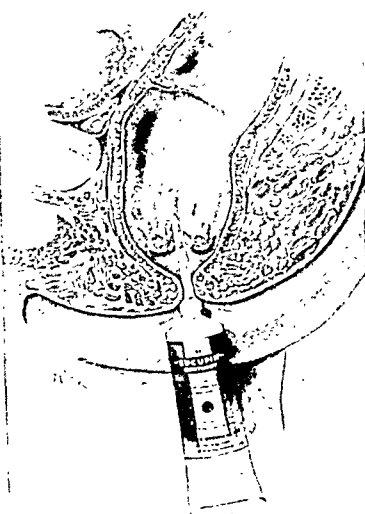
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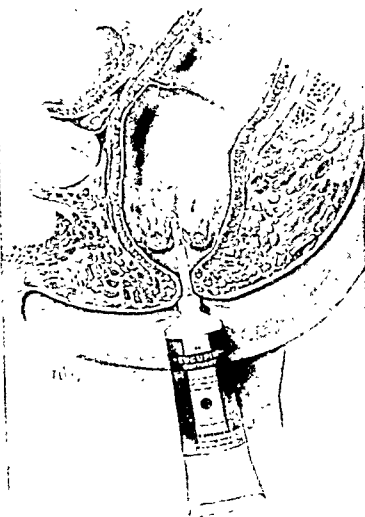
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TABLE OF CONTENTS ON PAGE 4

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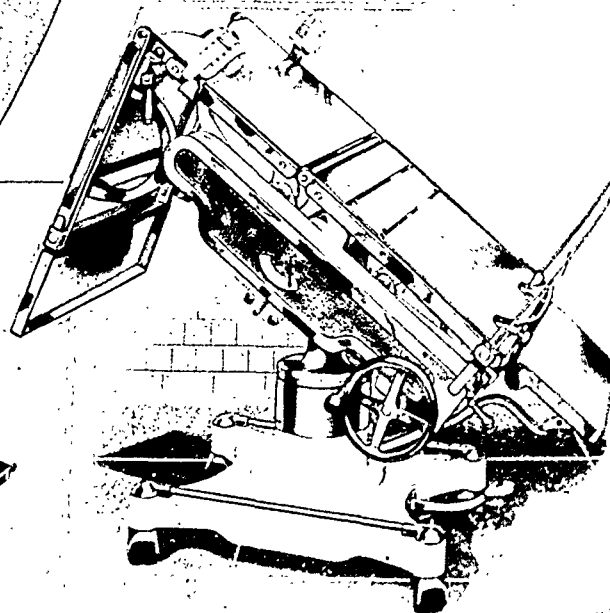
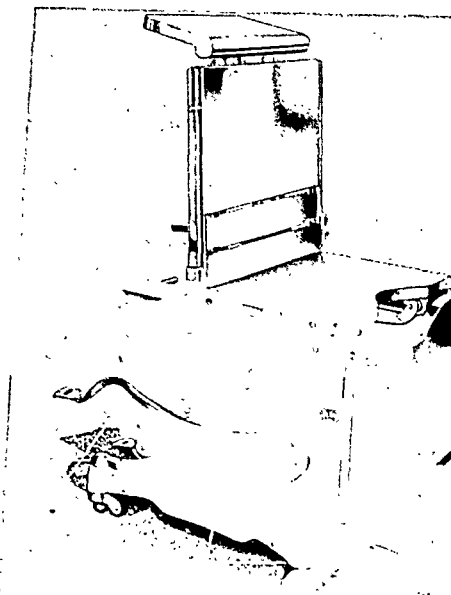
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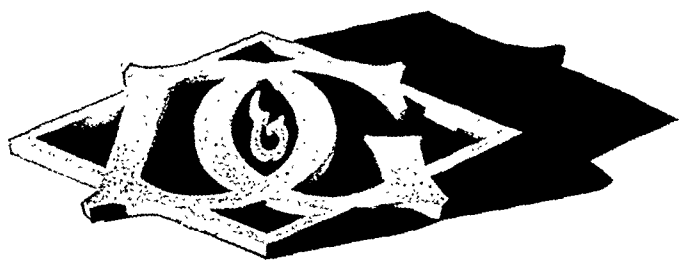
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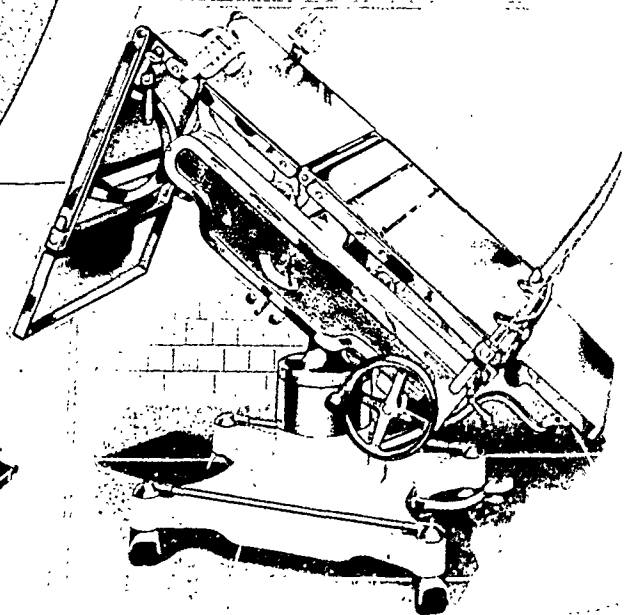
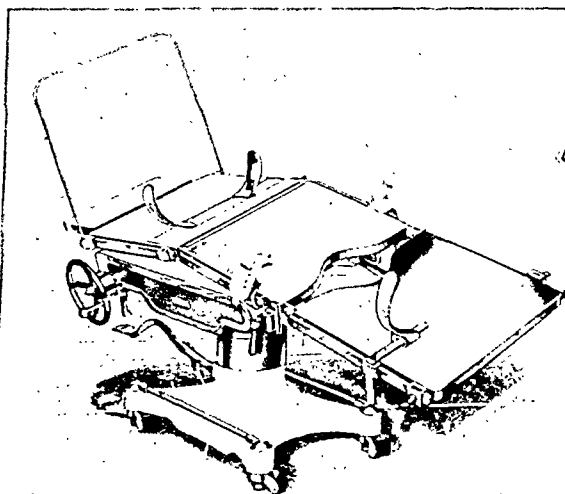
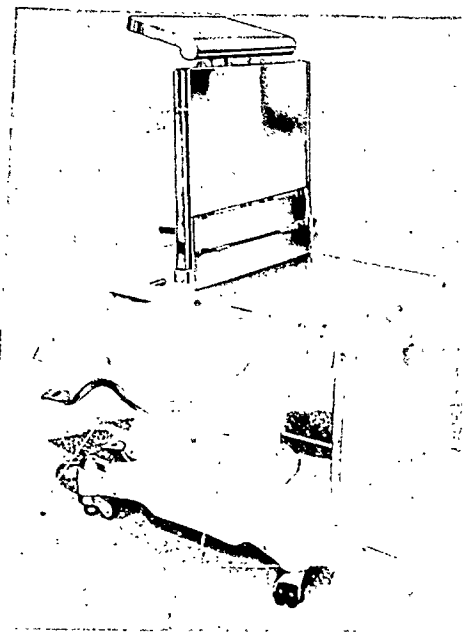
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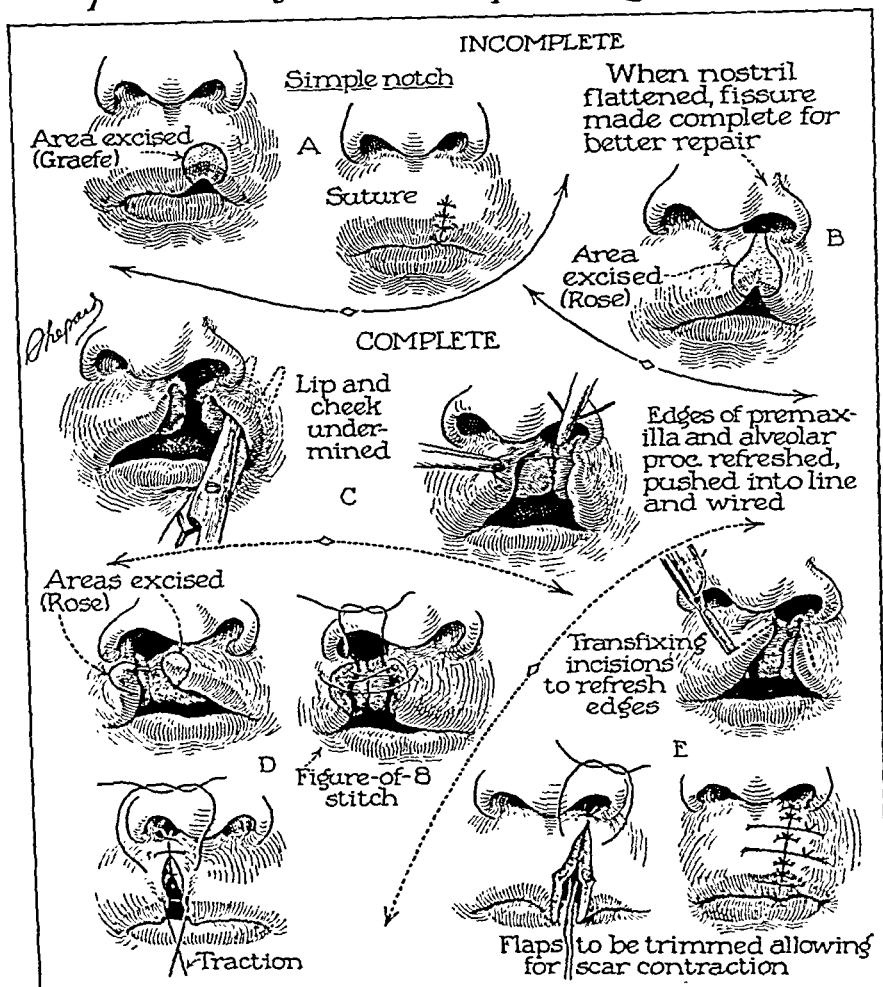
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PLATE NO. 78

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# SURGERY

## CONTENTS FOR FEBRUARY, 1938

### Original Communications

Operation on a Defunctioned Distal Colon. Sir Hugh Devine, M.S., F.R.A.C.S., Senior Surgeon, St. Vincent's Hospital, Melbourne, Australia	165
Acute Cholecystitis. Albert Behrend, M.D., and Howard K. Gray, M.D., Rochester, Minn.	195
A Reconstruction Operation for Distasis Recti. Leslie V. Rush, M.D., and H. Lowry Rush, M.D., Meridian, Miss.	200
Osteodystrophy of Unknown Etiology. Edward L. Compere, M.D., and Monroe Garrison, M.D., Chicago, Ill.	203
Spina Bifida Occulta. Harold F. Buchstein, M.D., and J. Grafton Love, M.D., Rochester, Minn.	215
Resection of the Elbow Joint. Arthur J. Davidson, M.D., and M. Thomas Horwitz, M.D., Philadelphia, Pa.	226
Extrascapular Apicolysis (Semb). Joseph W. Gale, M.D., and Peter A. Midelfart, M.D., Madison, Wis.	231

### Editorials

The Extrahepatic Biliary Tract as a Functional Unit. Edward A. Boyden, Ph.D., Minneapolis, Minn.	260
The Role of the Liver in Thyrotoxicosis. Willard Bartlett, Jr., M.D., St. Louis, Mo.	261

### Recent Advances in Surgery

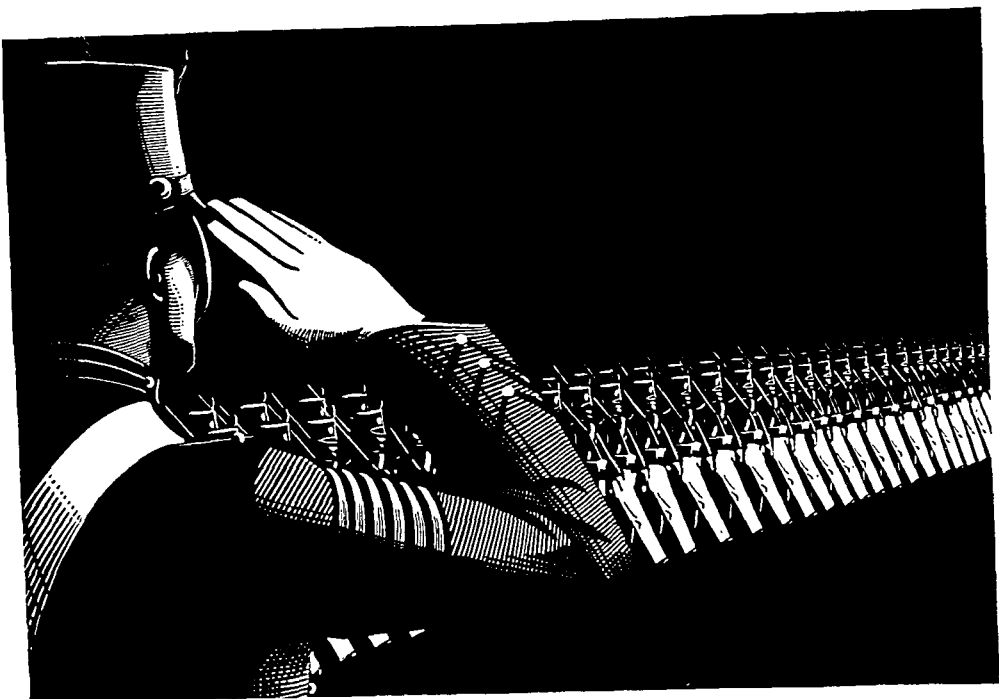
Congenital Arteriovenous Anastomosis. Stanley J. Seeger, M.D., Milwaukee, Wis.	261
--------------------------------------------------------------------------------	-----

### Review of Recent Meetings

Review of the Forty-Sixth French Congress of Surgery, Oct. 4-9, 1937, Paris. Adolphe Jung, M.D., Strasbourg, France	306
Review of the Meeting of the Association of American Medical Colleges, San Francisco, Calif., Oct. 25-27, 1937. C. D. Creevy, M.D., Minneapolis, Minn.	316
The Centennial Meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 20-22, 1937. Jennings C. Litzberg, M.D., Minneapolis, Minn.	319

### Book Reviews

Book Reviews	321
--------------	-----



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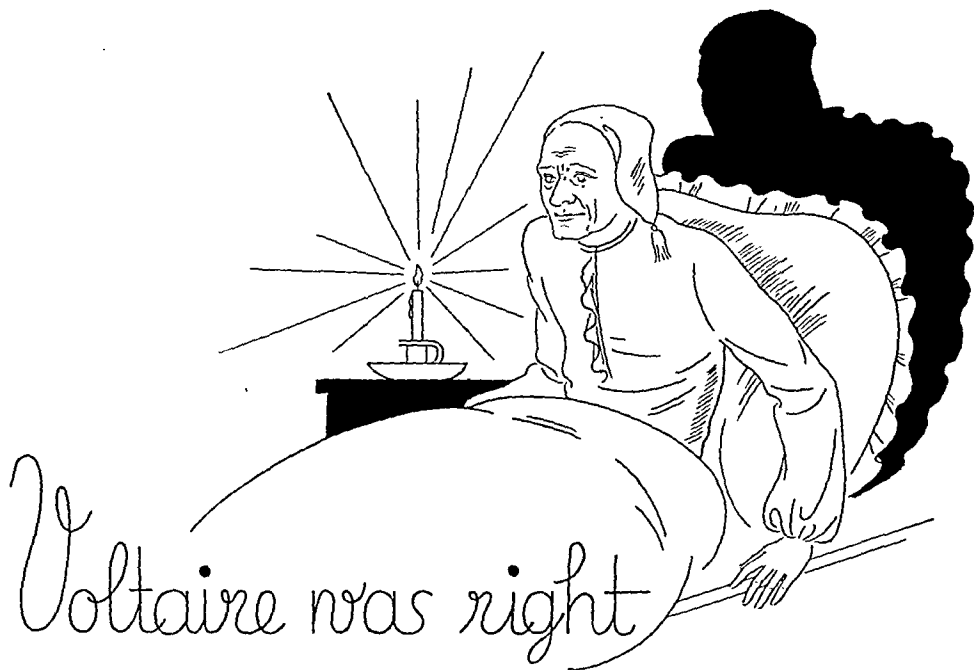
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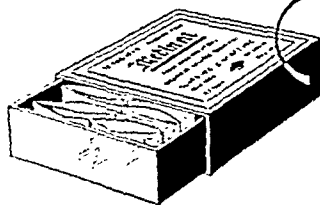
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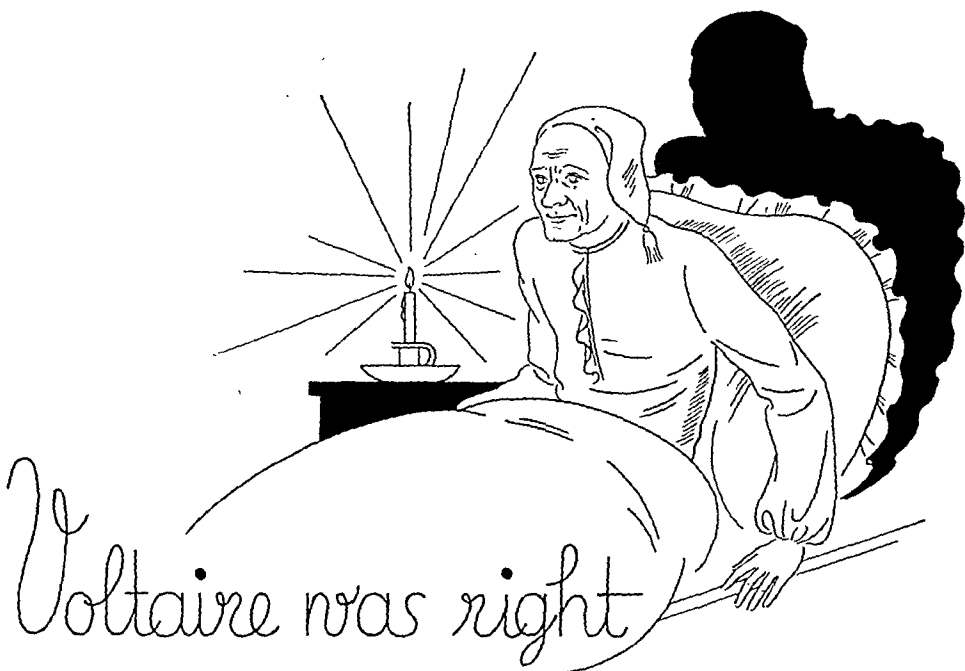


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# SURGERY

VOL. 3

FEBRUARY, 1938

No. 2

## Original Communications

### OPERATION ON A DEFUNCTIONED DISTAL COLON

SIR HUGH DEVINE, M.S., F.R.A.C.S., SENIOR SURGEON,  
ST. VINCENT'S HOSPITAL, MELBOURNE, AUSTRALIA

IN THE surgery of the distal colon, the principle of carrying out operations and allowing the wound in the bowel to heal in a distal colon which has been completely defunctioned has revolutionized my operative results in the surgery of this region. Not only has this method improved my results, but also it has enabled me to perform with success operations on the distal colon, such as the various forms of sutured anastomosis and anastomoses of the sigmoid to the rectum, operations which I never dared attempt in the functioning distal colon. The principle of operating on the defunctioned colon has, therefore, not only enabled me to save many lives, but also it has permitted me to save the continence of many patients, who, otherwise, with the ordinary system of operating, would have been left with artificial anuses.

By a defunctioned distal colon I mean one which has been completely disconnected from the alimentary canal, so that it cannot be soiled in any way by even the smallest quantity of feces; one from which the fecal contents have been washed out; and one which has been allowed to remain functionless until such time as the bacterial content has been considerably reduced—reduced on the principle that if, experimentally, a segment of bowel be completely isolated and thus deprived of its function, in the process of time, it will lose most of its bacterial content. The process of debacterialization—if I may coin such a word—brought about by the defunctioning of the distal colon and the lapse of time, can be hastened by daily lavage of the excluded segment, with saline solution, with solutions of low surface tension, or with weak antiseptic solution.

The two important points in this method of operating on the defunctioned distal colon are first that the operation is carried out under favorable conditions—absence of septic feces, functionless collapsed and retracted colonic walls, and low bacterial content; and second, that the

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of all to employ an operation, the danger of which was not great, I could not employ operations based on the principle of Paul.

In looking round for better methods for operating on the colon, and particularly on the distal colon, I was struck by the fact that it was its "cess-pool"-like function which was the great "stumbling-block" in its surgery. I felt that if I could deprive the distal colon of its function, remove its contents, let it lie dormant for some time until it had lost a good deal of its germ content, just as the isolated experimental loop lost its organisms, I could carry out any operation on it and get just as good repair in it as I would in any other part of the intestinal canal. And that is exactly what has happened: I have been able to carry out sutured end-to-end or side-to-side anastomoses in old and debilitated cancerous patients; to remove almost the whole of the sigmoid in inflammatory diverticular tumor and eventually join the upper part of the sigmoid to the upper part of the rectum; to remove carcinomas of the lower end of the sigmoid, and anastomose the middle of the sigmoid to the divided rectum; to remove inflammatory diverticular tumors of the sigmoid, which, by the ordinary methods of operating, would be quite irremovable; to remove a series of innocent adenomas of the sigmoid by slitting it longitudinally, dissecting them out of the mucous membrane, and then closing the lumen of the bowel; and to cure the rectovesical fistula arising from diverticulitis of the sigmoid.

A faithful adherence to this simple principle of operating on the distal colon has enabled me to excurse, with success, into fields of colonic surgery, into which I had never dreamed of wandering. It has, of course, reduced the mortality rate of my colon surgery to one which bears comparison with the mortality rate of my other operations in the abdominal cavity. I must admit, however, that this success has tempted me to explore realms of what I might call "derelict" colon surgery; that is, it has tempted me to operate on many hopeless-looking cases of carcinoma of the sigmoid, because I learned that after defunctioning the distal colon for some time, some growths that appeared to be inoperable lost their adhesions to surrounding structures, became smaller and operable. As one would expect, the excursion into this surgical field led to as many failures as successes. But the successes were absolute ones, for, otherwise, if the ordinary standards of colon surgery were followed, these cases would have been certain deaths; and the failures would have died under any circumstances.

#### THE APPLICATION OF THE PRINCIPLE OF OPERATION ON THE DEFUNCTIONED DISTAL COLON

In the surgery of the distal colon, there are two main fields: the surgery of malignant conditions, the main one of which is carcinoma of the sigmoid; and the surgery of innocent affections, which comprise inflammatory diverticular tumors with their complications, rectovesical



wound in the intestine is allowed to heal under these conditions. And of these two points, the healing of the wound in a bowel devoid of content and without function is much the more important.

Arising out of this method of operating is, what I consider, another advance in the surgery of the colon, and this is that the disconnection, to defunction the distal colon, which is made at the hepatic flexure or in the proximal part of the transverse colon, can be made more or less continently; that is, the patient need not be soiled with the fecal contents, nor need he wear a colostomy cup. The semifluid contents of the cecum and ascending colon can, as a rule, be "corked" into this segment of bowel, as if they were corked in a bottle—the patient can wear a corked tube fitted into the small fistulous opening which serves as a disconnecting anus. The contents of the cecum can then be emptied or evacuated by a "wash-out" every twenty-four hours. As a rule, there is very little soiling of the abdomen, rarely any irritation of the skin, and never any smell. I have never been able to obtain the same degree of continence and the same degree of comfort with an opening in the sigmoid region, that is, with the ordinary artificial anus.

In the past, like most surgeons, I was very worried over the result of my surgery in the region of the distal colon. No matter how carefully and aseptically and skillfully I made an anastomosis in the distal colon, the mortality rate of these operations was high—as high as 30 per cent. I soon learned the value of draining the bowel by cecostomy or some other means as a preparation for a resection and an anastomosis; but although the results were better, the operation on the still dirty, perhaps functioning, bowel, and the healing under the same conditions, especially in a metabolically diseased, anemic, and toxic cancer patient, were still attended with a considerable mortality rate—a mortality rate too high to be tolerated in these days of successful surgical operations.

In an effort further to improve my results, I resorted to all sorts of modifications of Paul's technique. In cases of carcinoma of the sigmoid or of the transverse colon, so favorably situated that this operation could be carried out, my results were most successful; indeed, no better results could be desired. But the difficulty with this method was that it was so successful that I was tempted to employ it for growths in the upper or lower part of the sigmoid—positions which were not favorable to its performance—and I found that I was not removing enough of the mesentery. And as a consequence of this, the remote results results which, in the more or less favorable carcinoma of the colon, should be good—were not all that could be desired. I found, too, that this method was of very little use in the inflammatory conditions of the sigmoid; that is, in conditions such as large inflammatory diverticular tumor of the sigmoid, in which the whole sigmoid was involved, and in which the mesentery and the bowel were rigid and contracted. In such circumstances, that is, in an innocent condition, in which I needed most

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It is in what I have termed the "derelict" phases of carcinoma of the sigmoid colon that this method is of great advantage. A distal colon can be defunctioned for a month. The growth can then be resected, and the divided end of the functionless sigmoid implanted in the upper and lower end of the wound—an operation of little severity and danger. The patient may then be sent home for twelve months. During this time, he will be able to live a fairly normal life, because his disconnecting anus will be more or less continent and he will, therefore, be able to carry out his usual work. Thus, adequate time—a most important factor—is allowed for improvement of his general and local conditions. His general condition should greatly improve, because, his growth being removed, he will be free not only from the systemic toxic infection of the growth itself, but also from that caused by his chronic intestinal obstruction. Any systemic metastasis, which might not have been obvious at the operation, will become manifest. Locally, the bacterial content of his colon will have greatly decreased, and the vascularity of the bowel wall, particularly that in the divided ends, will have become definitely established. Thus, a sutured anastomosis of the colon segments—the dangerous part of an operation for the removal of a malignant growth in the colon—can be carried out under such ideal general and local conditions that there should be no more danger to the patient than that of any other abdominal operation.

*The Method of Operation on the Defunctioned Distal Colon.*—This method of operation on the defunctioned colon involves the following:

1. A complete disconnection of the proximal from the distal part of the colon, so that the distal colon can be completely defunctioned.
2. A preliminary exploration of the abdomen.
3. The construction of a disconnecting anus, which
  - a. completely disconnects,
  - b. is more or less continent,
  - c. can be easily closed,
  - d. is situated well away from the area of the operation.
4. The preparation of the defunctioned distal colon.
5. The type of operation carried out on the defunctioned distal colon.

*The Complete Disconnection of the Proximal From the Distal Colon.*—It is important that the distal colon be completely disconnected from the rest of the alimentary canal. The ordinary spur colostomy does not bring about a permanent complete disconnection; for its spur soon begins to draw in when some fecal contents follow the plane of the mucous membrane and soil the distal segment. Complete disconnection is obtained by cutting the bowel across and inserting the ends into separate openings in the abdominal wall. The disconnection is made in the proximal limb of the transverse colon; or if the transverse colon be short, at the hepatic flexure.

fistulas, etc., single or multiple adenoma of the sigmoid, and endometrioma of the lower part of the sigmoid or the rectosigmoid junction.

Of these two fields of surgery, the one concerned with inflammatory conditions of the distal colon gives the most dramatic results, because on account of their innocency time is not a factor. And furthermore, on account of a reasonable amount of continence in the disconnecting anus, and, therefore, because discomfort and invalidism are not considerations, patients are not in the least disturbed by the defunctioning of the distal colon for a year or two. Thus, the distal colon can be defunctioned until such time as the bowel is almost germ-free and all inflammation has disappeared, and even until most of its effects on the tissues have been repaired.

In the field of malignancy, time is a great factor, and the distal colon cannot be defunctioned (and prepared) for a period any longer than three weeks or a month. But, in this field, there has been this advance: it is the septic character of the contents of the normal colon which constitutes the main danger in its surgery. In the carcinomatous distal colon, this septic character is increased many fold because it is chronically obstructed; for scarcely any carcinoma of the colon comes to the surgeon before it exhibits symptoms—colicky pains and distention—which are those of chronic intestinal obstruction. Thus, in the carcinomatous distal colon, the pathogenicity of the bacterial contents of the colon is greatly increased, the colonic walls are thin and their thin walls are almost permeable by germs, its lymphatics are full of infective organisms and its tissue vitality toxically spoiled—all conditions in which an operation would almost certainly lead to peritonitis, and in which repair could scarcely be expected. In such circumstances, complete defunctioning of the distal colon, especially when it is prepared by daily lavage—even if it be for the short period of a month—brings about such a profound change in the pathogenicity of the bowel contents, and in its walls, that the mortality rate of operations in the carcinomatous colon is greatly reduced. Not only does the short period of defunctioning improve the local resistance of the patient's colonic tissues, but also the patient's general resistance. It certainly permits the growth to be removed with safety. But repair, after an anastomosis between the segments, although ever so much safer than in other methods, is nevertheless not so safe as the repair of anastomosis when it is allowed to take place in a distal colon which has been defunctioned for many months.

Even in the malignant field, however, it is possible to take full advantage of this principle of operation on a defunctioned colon, for the reconstitution of the continuity of the bowel—the dangerous part of colonic operations—can be made in a colon which has been defunctioned for any desired period; and thus, the immediate results of the surgery of malignant conditions can be made almost as safe as those of innocent conditions.

it should be capable of being easily closed, and (4) that it should be situated well away from the area of the operation. The first is obtained by dividing the bowel and implanting the divided ends into separate openings in the abdominal wall; the second, by making a small fistula-like anus at the beginning of the transverse colon with an opening so small that it can be easily occluded; the third, by combining the small fistulous anus with a very long spur; and the fourth, by making the disconnection in the upper right part of the abdomen at either the proximal part of the transverse colon or the hepatic flexure.

*The Steps in the Technique.—*

1. The incision: Already described and used for exploratory purposes; two and one-half inches long in the upper part of the right rectus.

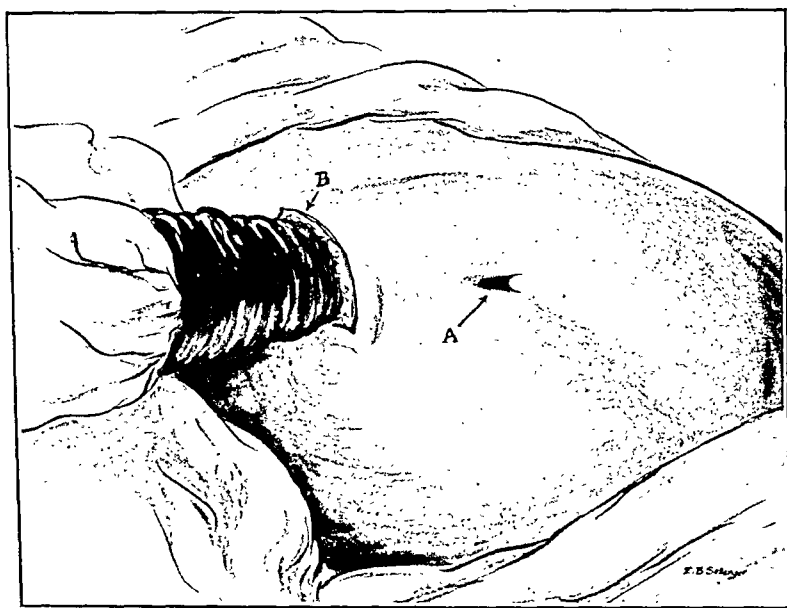


Fig. 2.—Drawing, made from photograph, of an exploration of the abdominal cavity, being made through this small incision, with a vaselined gloved hand. The drawing shows the operation viewed from the end of the table. A is the umbilicus; B, gloved hand inserted into the small exploratory incision through which the disconnecting anus will be made.

2. Formation of the long spur: If the transverse colon be long, its proximal part is drawn out of the abdominal wound and a tube passed through the apex of the loop as shown in Fig. 3. The loop is now stretched to its full extent, and its limbs are connected together by a running suture, so as to make as long a spur as possible (Fig. 4). The spur should be four or five inches long. If the transverse colon be short, the long spur is made by suturing the proximal part of the transverse colon to the ascending colon, the apex of the loop then being the hepatic flexure.

3. The parietal peritoneum is sutured round the neck of the loop (Fig. 5).

*Preliminary Exploration of the Abdomen.*—Advantage is taken of the slight first-stage operation of making a disconnecting anus, for the purpose of defunctioning the distal colon, to make a preliminary exploration of the abdomen. An incision a little over two inches in length is made in the upper part of the left rectus muscle (Fig. 1). This incision is preferably made very small, because through it the disconnecting anus is going to be made and therefore it may become infected; and in the presence of infection, a small wound is more manageable and less dangerous to the patient than a large one. Exploration of the whole abdomen through this small opening can be most effectively carried out by vaselining the gloved hand (Fig. 2). The lubricated gloved hand slips

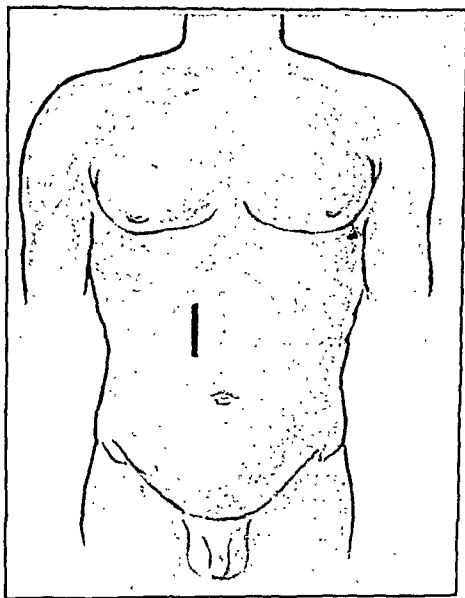


Fig. 1.—Showing the position of the small incision made over the upper part of the right rectus muscle. Note the smallness of the incision (about  $2\frac{1}{4}$  inches).

readily through the small incision; the omentum or intestines do not cling to it, and thus, an exact and reliable exploration of the growth, the liver, and of the whole abdomen can be made. With this simple aid, it is surprising to experience, for the first time, the comfort and ease with which an exploration, usually difficult under such circumstances, can be carried out.

The main object of the exploration is to make an examination of the growth and of any glandular involvement with a view to its operability, and to ascertain if there is any metastatic spread of the growth, which would prohibit its radical removal.

*The Construction of the Disconnecting Anus.*—In regard to this disconnecting anus, there are four requirements: (1) that it should completely disconnect, (2) that it should be more or less continent, (3) that

bowel ends are now sutured, so as to make a pair of tiny fistulas, for it only requires a very small opening to allow egress of the semifluid

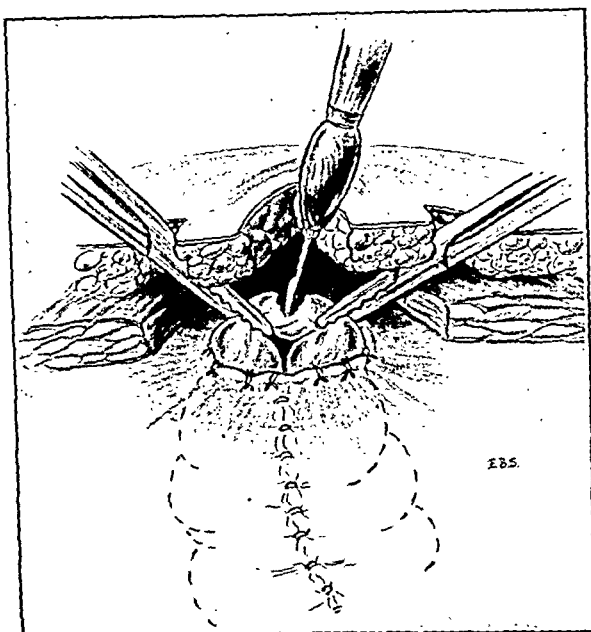


Fig. 5.—Kocher clamps applied to the bowel through two small openings in the abdominal wall, which do not include the muscle of the abdominal wall.

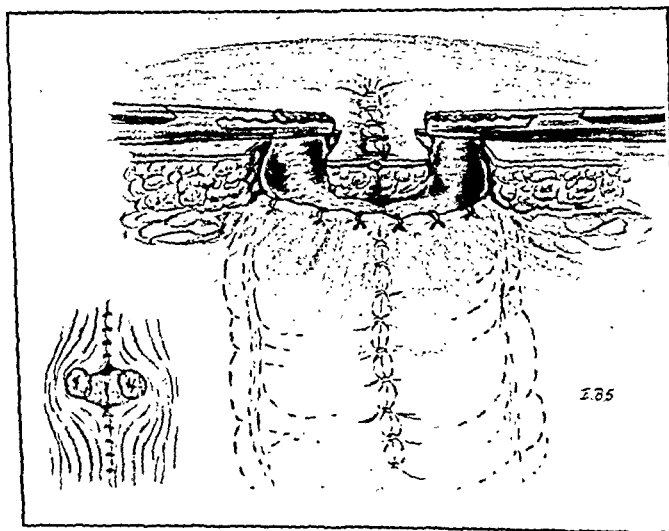


Fig. 6.—Diagrammatic section to show the two cut ends of the bowel drawn up through the small openings by the Kocher clamps, and the main wound sutured. Inset shows position of muscle in relation to the ends of the bowel.

contents of the ascending colon, and there is very little danger of the fistula closing, because, from its nature, it must always function.



4. Button-hole openings (through only part of the abdominal wall) are made one inch on each side of the incision. Through these openings, Kocher clamps are applied to the bowel (as in Fig. 5), which is then

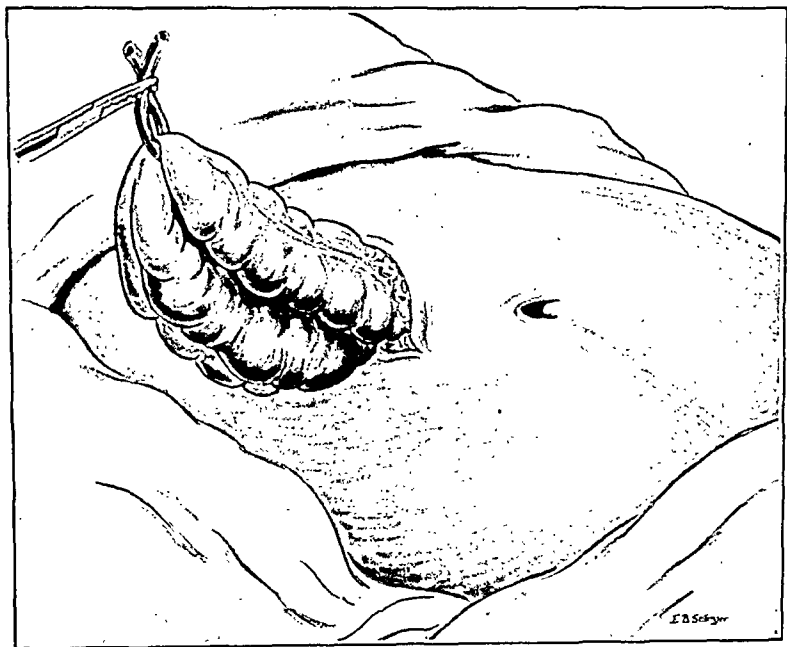


Fig. 3.—Proximal part of transverse colon drawn out of the abdominal wound and a tube passed through the apex of the loop.

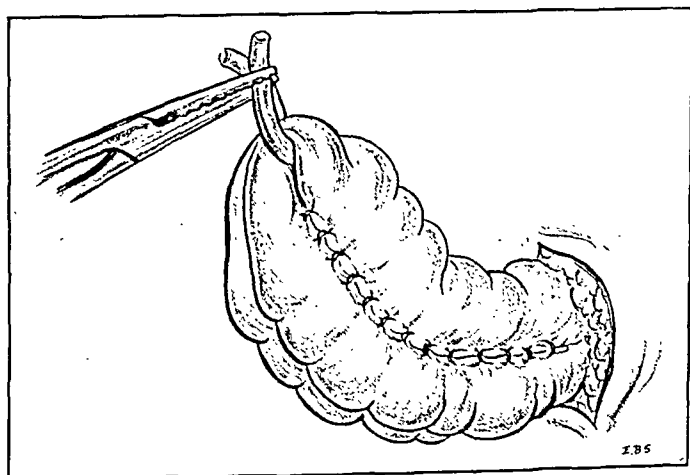


Fig. 4.—Running suture connects the limbs of the loop.

divided, between them, with a diathermy knife, and its cut ends, after being coagulated with the diathermy current, are drawn by the forceps into the button-hole openings (Fig. 6). The skin edges around the

Thus, this technique produces an anus giving all requirements: complete disconnection; the small opening which is easily occluded but through which the semifluid contents of the cecum and ascending colon can discharge; the very long spur, the crushing of which permits early restitution of function; the anus situated well away from the region of the future operation. Fig. 8 is a drawing showing how small is the finished disconnecting anus. Very rarely in a case of acute intestinal obstruction, the bowel is so intensely distended that it is impossible to



Fig. 9.—Photograph which shows how small these colostomy openings can be, and yet function properly.

make a spur. In these circumstances, a cecostomy should be made and when the bowel regains its normal size, a disconnecting anus can be made.

*Management of the Disconnecting Anus.*—Fig. 9 is a photograph which shows how small these colostomy openings can be, and yet function properly. One surgeon, on whom I carried out this form of colostomy, was able to control the bowel contents for twenty-four hours with a toy balloon. He then took it out, leaned over a dish, emptied his bowel, cleaned the anus, and put back the balloon, and he would then be free from fecal discharge for another twenty-four hours.

In order that there should not be the slightest intestinal obstruction with such a small anus, the proximal Kocher clamp is taken off after

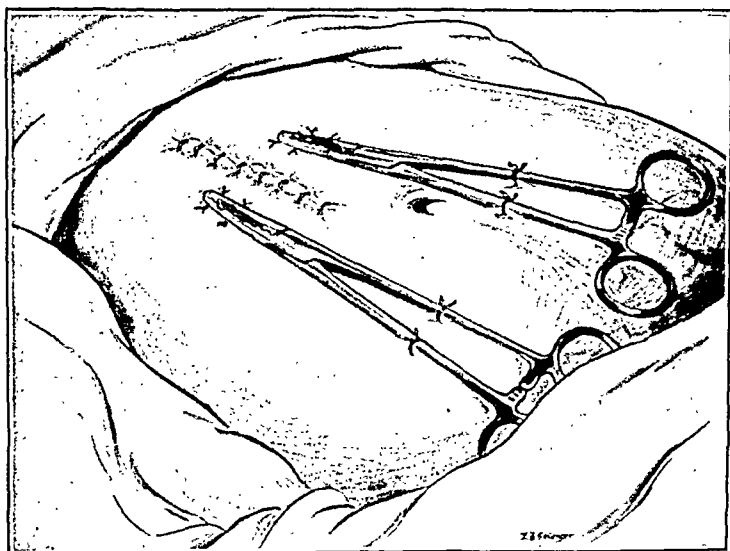


Fig. 7.—Kocher clamps in position on the abdomen.

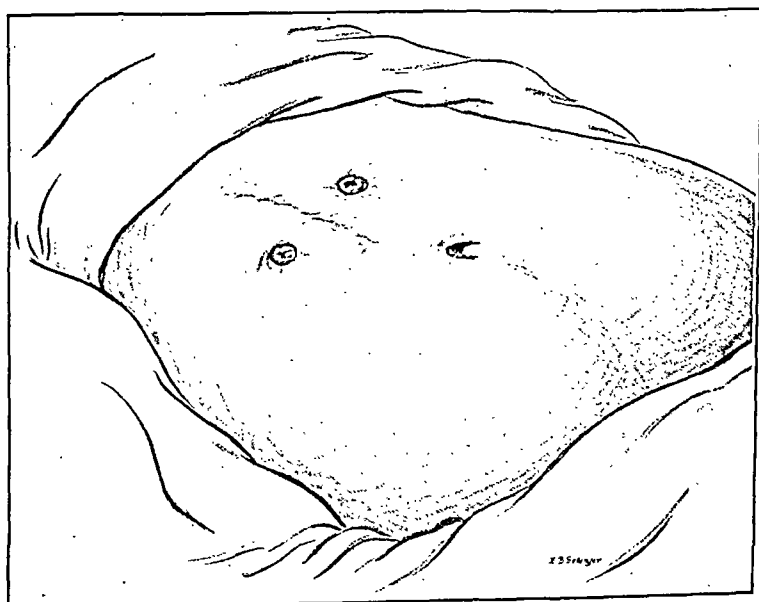


Fig. 8.—Shows the disconnecting anus.

twelve hours, but in order to keep the bowel ends in proper position, the distal one is left on for several days. Fig. 7 shows the two clamps in position on the abdomen.

colon, it is now conceded by those surgeons who have had experience in the surgery of the colon that it is unsound and dangerous to use this form of anastomosis in connecting up the distal colon after resections.

The difficulties and dangers of a sutured anastomosis in the functioning distal colon are:

1. The contents of the colon are very infective, and, as during the operation the lumen of the bowel must be opened, it is almost impossible

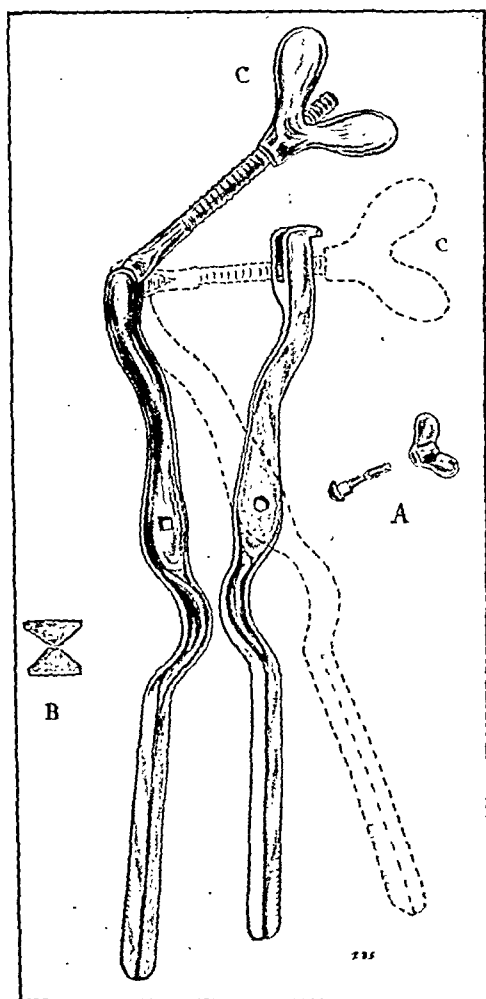


Fig. 13.—An illustration of the enterotome, with its blades disconnected. *A* indicates the screw which connects the two blades; *B*, a cross-section of the blades; *C*, the large winged nut which draws the two blades tightly together after they have been placed in position on the spur and connected.

to prevent soiling of the peritoneum and, therefore, the occurrence of some grade of peritonitis.

2. The natural vascularity of the colon is so poor that it is never certain that the cut ends of the bowel, with the added embarrassment of sutures, have sufficient circulation to ensure proper repair.

an illustration of the enterotome. The blades are vaselined before use, introduced separately, and then connected up with the screw *A. B* is a cross-section of the blades. Fig. 14 is a diagram showing the enterotome applied.

Through the deep anastomosis formed by this long enterotome, all the fecal contents pass, rather than up through the fistula-like anus. The consequence is that, except for a small fistulous opening, which may discharge a little feces or perhaps only air, function is restored in a few days.

The small fistulas can be closed with a local anesthesia, but very often they close naturally.



Fig. 12.—The enterotome in position.

*The Type of Operation to Be Carried Out on the Defunctioned Distal Colon.*—

1. Partial sigmoidectomy with sutured anastomosis.
2. A rectosigmoid resection with sutured anastomosis.
3. Rectosigmoid resection with telescopic anastomosis.
4. Extensive sigmoidotomy for the removal of single or multiple adenoma.

*Sutured Anastomosis in a Functioning Distal Colon.*—Whatever may be the opinion in regard to the soundness of making a sutured anastomosis in reconstituting the bowel after an ileocolic resection of the proximal

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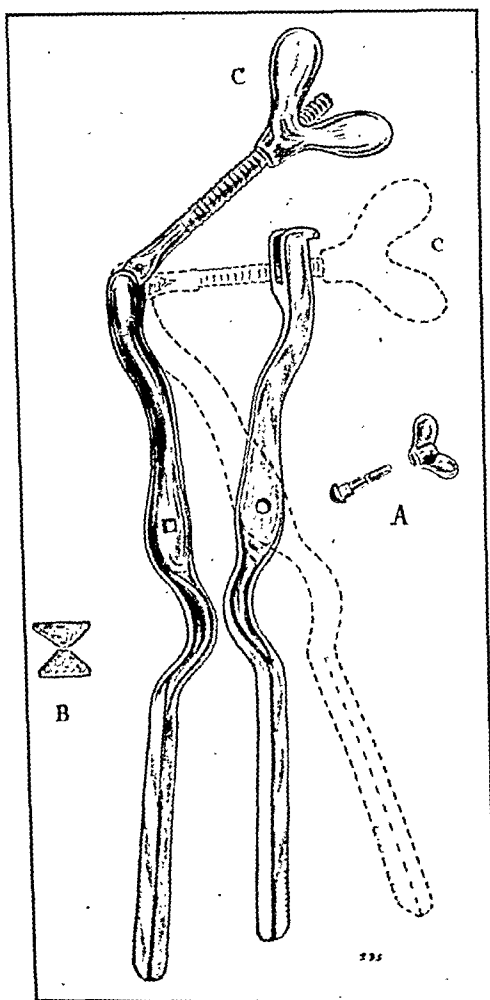


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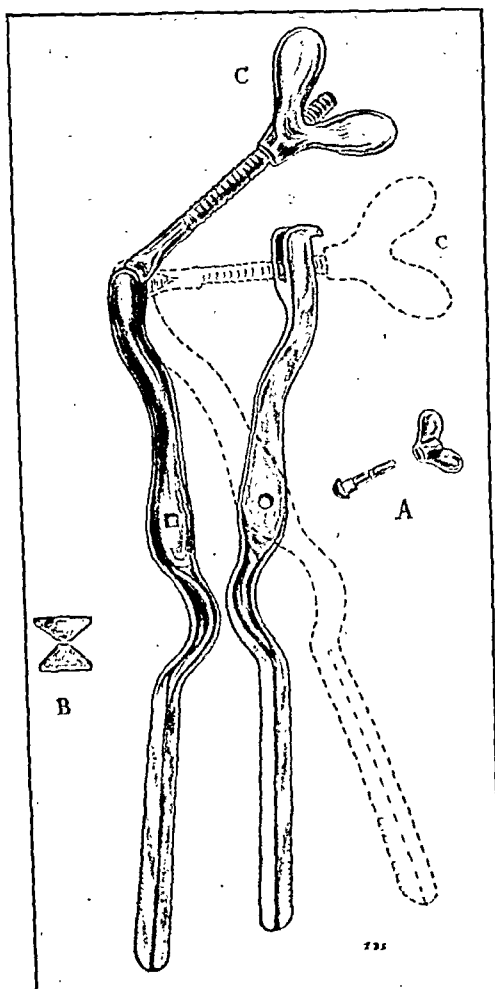


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3. The repair of the peritoneal layer of the colon is not effective as in the small intestine. Infection from the colonic contents is very likely to leak to the peritoneum through the actual line of contact of the segments of bowel; it may also pass through little areas of necrosis in the cut edges of the bowel, which occur from a suture pressure in the poorly vascularized colonic wall; or it may pass along the sutures.

Wilkie recognizes the danger of making a sutured anastomosis on orthodox lines in the distal colon. Using but one layer of interrupted sutures through the seromuscular coat only, he places his sutures and ties them with great care, so to avoid any tension, and therefore any interference with the vascularity of the cut ends of the bowel.

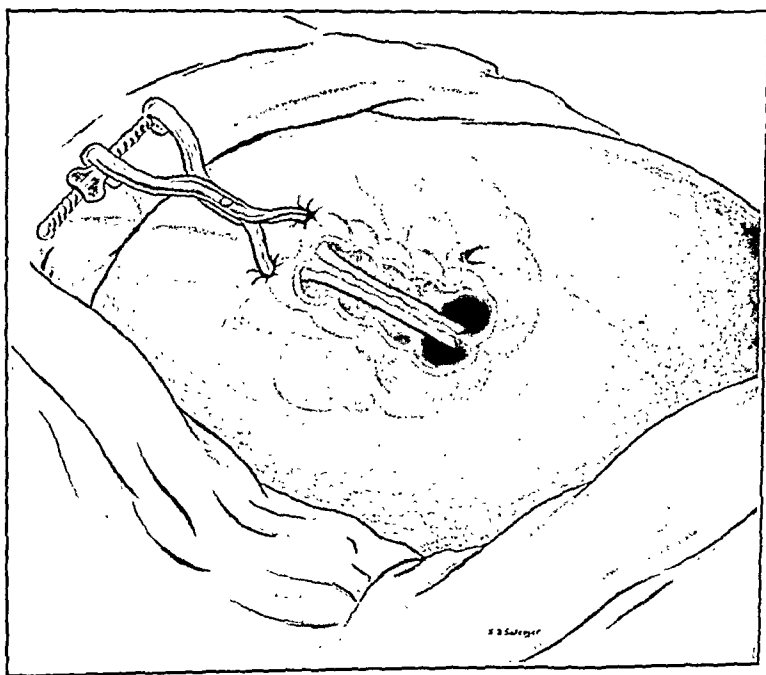


Fig. 14.—Diagram showing the enterotome applied. For diagrammatic purposes the abdominal wall in the drawing is considered transparent and the spur semisectional.

The various methods of so-called "aseptic anastomosis" cannot possibly be aseptic. Furthermore, in these methods the liability of infection along the sutures is still present and the dangers attendant on defective blood supply are not obviated. Finally, it may be accepted as a clinical fact that a sutured anastomosis made in the functioning distal colon involves a high percentage of mortality.

*How Soon Should Operation Be Carried Out on the Defunctioned Colon.*—The longer the distal colon has been defunctioned, the lower the bacterial content and the better the local condition. In innocent conditions, such as a diverticular tumor or the complications arising from it, operation may be delayed for twelve months. In such inflammatory

conditions, long defunctioning is sound treatment, because areas of inflammation, spreading from the tumor, resolve; and extensive adhesions, which may bind the inflammatory tumor to all the organs in its neighborhood, slowly disappear. But not only does a prolonged defunctioning of the distal colon enable the surgeon to remove inflammatory tumors, which previously were inoperable, but also it avoids for him the removal of bowel, which is inflamed, but otherwise healthy. In one patient, who developed acute intestinal obstruction as the result of an inflammatory diverticular tumor in the sigmoid, the diverticular condition completely cleared up after the distal colon had been defunctioned for twelve months, and normal function was restored to the patient. In another patient in whom I had unsuccessfully made two attempts to remove an inflammatory diverticular tumor in a defunctioned distal colon, I was able eventually, after the bowel had been defunctioned for a considerable time, to remove the tumor. Thus, in innocent affections, the longer the distal colon is defunctioned, the safer and more successful is the operation.

In malignant conditions, anyway, as far as the removal of the growth is concerned, the bowel cannot be defunctioned for more than a month. The operation for the reconstitution of the continuity of the colon can, however, be always carried out in a bowel in which a long period of defunctioning has been allowed. It is surprising to see the effect that defunctioning has on some malignant growths. In two instances where malignant tumors of the sigmoid appeared to be quite inoperable, because they were widely adherent to surrounding structures, I found that after a period of four months of defunctioning, they became operable. Only a small proportion of malignant growths, which appear to be inoperable, however, behave in this way, for it is only in a few cases that the extensive adhesions, which make them inoperable, are the result of an associated inflammatory condition arising from an ulcerating cancer tumor.

*Partial Sigmoidectomy and Sutured Anastomosis in a "Defunctioned" Distal Colon.*—In the defunctioned distal colon, which is quiescent, retracted, and clean, it is possible safely to perform an orthodox sutured anastomosis; and it is still possible to do so even when the segments of bowel to be anastomosed are incompletely peritonealized, or when the disparity in their caliber is great. The use of a sutured anastomosis in the case of carcinoma of the upper and lower parts of the sigmoid is of great advantage, for the requisite amount of bowel which should be removed with the carcinoma and the proper amount of pertaining mesenteric leaf can be critically estimated and then removed—an advantage which does not obtain in operations on the principles of Paul, Mikulicz, and others.

The healing of a sutured anastomosis in a defunctioned colon takes place under favorable conditions; that is, under conditions of complete rest—a most important surgical principle. The postoperative

course after these operations is uncannily uneventful—an indication of the absence of even mild grades of local peritonitis, and therefore of any degree of infection.

In the defunctioned distal colon, a real "aseptic" anastomosis can be made. This is made possible by the fact that the lumen of the "defunctioned" colon can be aseptically sealed by diathermic coagulation, and it does not matter when it opens. The method of making this "aseptic" anastomosis is illustrated in Figs. 15 and 16. The segment of bowel containing the growth is isolated with the aid of the diathermy knife and

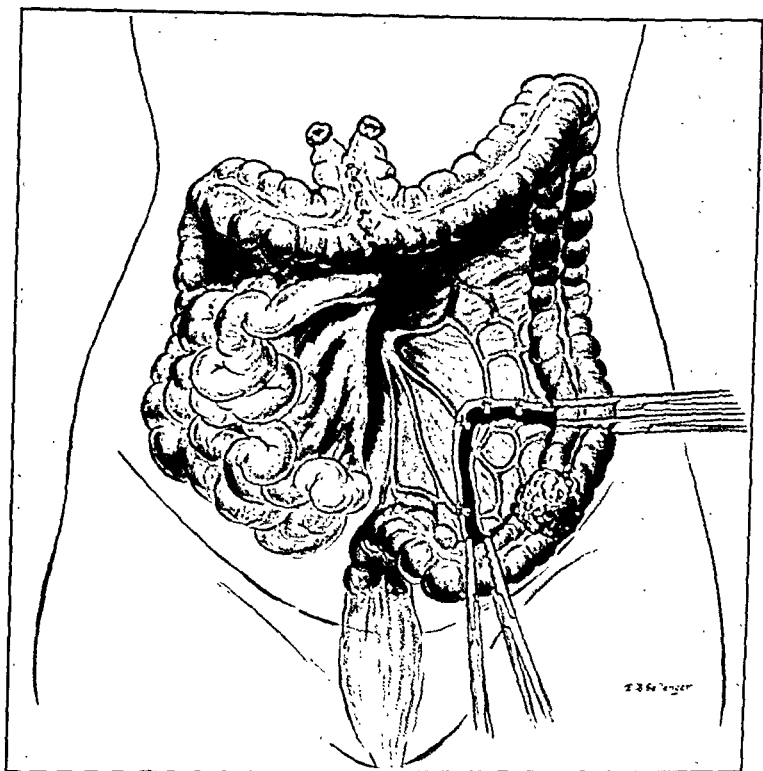


Fig. 15.—Resection of a defunctioned distal colon.

Kocher clamps, and with the corresponding part of mesenteric leaf removed (Figs. 15 and 16). The Kocher clamps closing the proximal and distal segments are then contacted with the diathermy current in order to coagulate that piece of bowel which lies within the grasp of the clamp. These forceps are then approximated as shown in Fig. 16. Interrupted sutures taking in a big bite of the seromuscular layer are now placed round the whole circumference of the bowel ends, as shown in Fig. 16. These sutures are tied so gently that the sealed ends of the bowel are not opened. The rent in the mesentery is closed in the usual way. The segment of bowel containing the anastomosis should, for additional

safety, be embedded in a little pocket of omentum. A drainage tube is inserted down to the anastomosis.

*Sigmoidotomy for Removal of Single and Multiple Adenoma.*—In cases where there have been large single or multiple adenomas, after defunctioning the colon for a considerable period, I have not hesitated widely to slit up the sigmoid and remove the adenoma. It is a comfort to feel that there is very little danger of a suture insufficiency in the extensively sutured sigmoid because the operation has been carried out on the defunctioned colon.

*Rectosigmoid Resection With Sutured Anastomosis.*—It is in growths in the lower third of the sigmoid that this method of operating on the

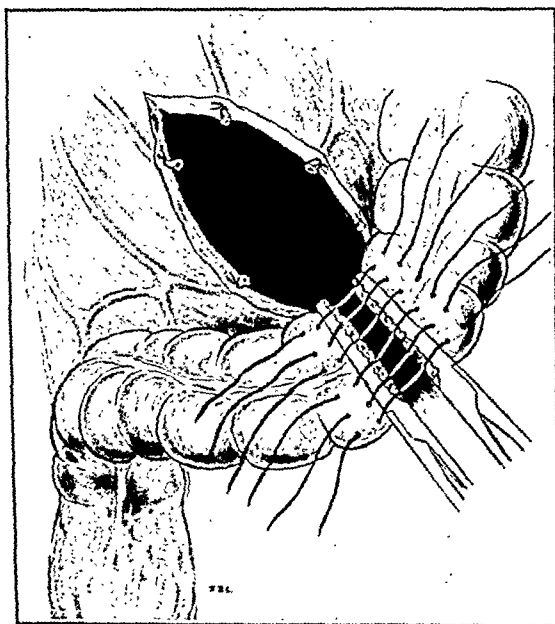


Fig. 16.—Resection and sutured anastomosis in a defunctioned distal colon.

defunctioned colon is so valuable. In this situation, any operation methods based on the principle of Paul cannot be satisfactorily carried out because they do not permit an adequate resection of the mesenteric leaf; and they do not allow sufficient removal of the bowel on the rectal side of the growth. Where, however, the operation is carried out on a defunctioned bowel, the proper amount of the sigmoid and upper part of the rectum with the corresponding part of the mesenteric leaf can be resected; and, with every prospect of success, and with very little danger, the sigmoid can be anastomosed to the divided rectum. When the repair of this rectosigmoid anastomosis takes place in a defunctioned colon, the incomplete peritonealization of the rectum does not mar the eventual successful healing of the anastomosis.

*Steps in the Technique of Abdominal Rectosigmoid Resection.*—The sigmoid is divided, between clamps (Fig. 17) well above the growth, and the mesentery, with its vessels, is also divided as in Fig. 15. The clamp is nearly three-quarters of an inch wide and has deep serrations so that it can get a very powerful firm grip on a piece of the cut segment. With great pressure, and the broad grip, and the coagulation of the gripped tissues by means of the diathermy current, leakage is impossible and the occluded end is absolutely sterile. This form of clamp is a convenient one for aseptically and hermetically sealing the divided ends of the colon. It can be allowed to lie uncovered in the abdominal cavity. It also serves

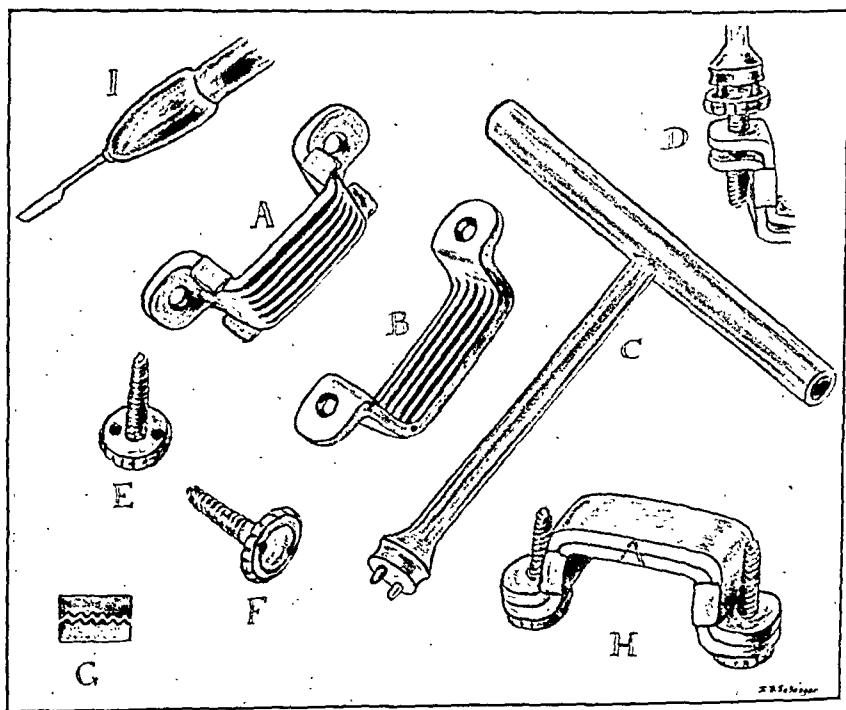


Fig. 17.—An illustration of what I call the "box clamp," which I use for closing aseptically the divided ends of the colon. A and B are the two sections of the box clamp; C, the key which is inserted into the screws E and F to bring the two sections of the clamp together with great pressure; D, the key in action; G, a sectional drawing which shows the serrations on the gripping surfaces of the two sides of the clamp; H, the box clamp assembled; I, the diathermy knife which is used to divide the bowel and to coagulate the cut edges of the bowel.

as a handle wherewith to make tension on the bowel when dissecting it from adhesions or out of the pelvis. Fig. 17 is an illustration of the clamp which I use for closing aseptically the divided ends of the colon.

The bowel is divided with a diathermy knife between an intestinal clamp above and a box clamp below flush with the edge of the latter clamp. The tissue at the edges of the box clamp and grasped by it is sterilized by contacting the clamp and its edges with the coagulating diathermy current. Holding the lower sigmoid segment by the box

clamp, the operator draws it forcibly upwards, puts its rectosigmoid peritoneal reflection on the stretch and divides it. The upper half of the rectum is now isolated by dissecting it from the pelvic wall laterally and from the bladder anteriorly, by means of a long spade dissecting scissors. (Fig. 18.) The rectum is divided in much the same way as the vagina is divided in the course of a panhysterectomy, and, as in this operation, a Wertheim's vaginal clamp is used to close the lower end of the rectosigmoid segment (Fig. 19). A clamp is not applied to the rectal stump

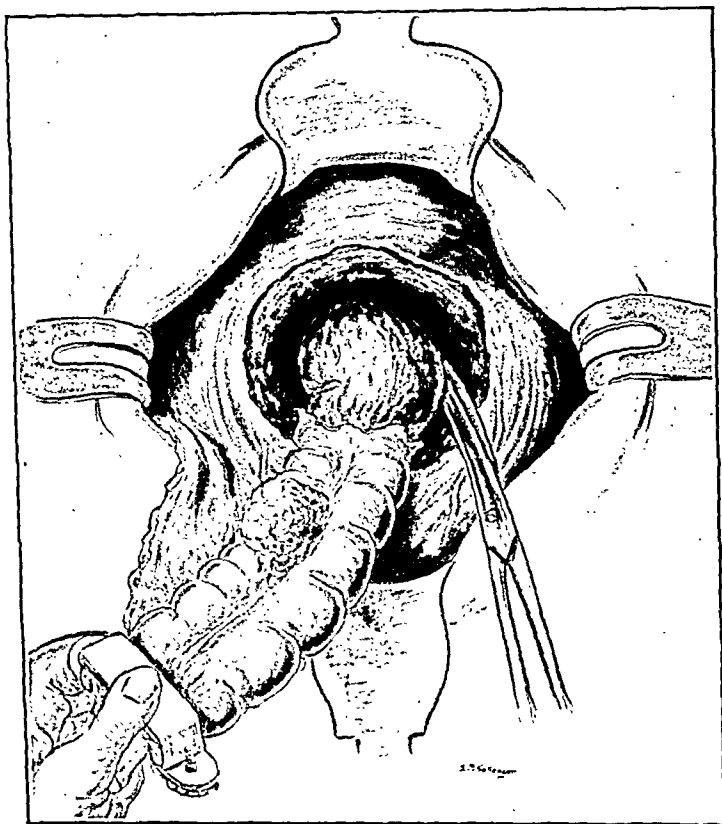


Fig. 18.—Isolating the upper half of the rectum, by dissecting it from the pelvic wall laterally and from the bladder anteriorly, by means of a long, spade-ended dissecting scissors.

because the tissue of its cut edges must not be crushed. Its use is unnecessary, as the rectum can be cleaned and sterilized, as far as it is possible, through the anus.

In the case of a woman, the tubes should be removed, because even the presence of slight infection (a mild sepsis occasionally occurs round the cut edge of the rectum) may give rise to tubo-ovarian abscesses.

The lower end of the sigmoid is now anastomosed to the stump of the rectum in the following way. The cut end of the sigmoid is examined, to make sure that it is properly vascularized. It is brought down to

the rectal stump, placed in the correct apposition to it, and secured in this position by guy-rope sutures, which, besides fixing the segments together, are used to anchor them to the operating frame. (Fig. 20.) As the bowel segments are empty and clean, interrupted sutures of fine, slightly hardened gut, taking a bite of about a third of an inch, are inserted from their lumens. These sutures are used to join the posterior and lateral walls, until it is impossible to insert any more. When this

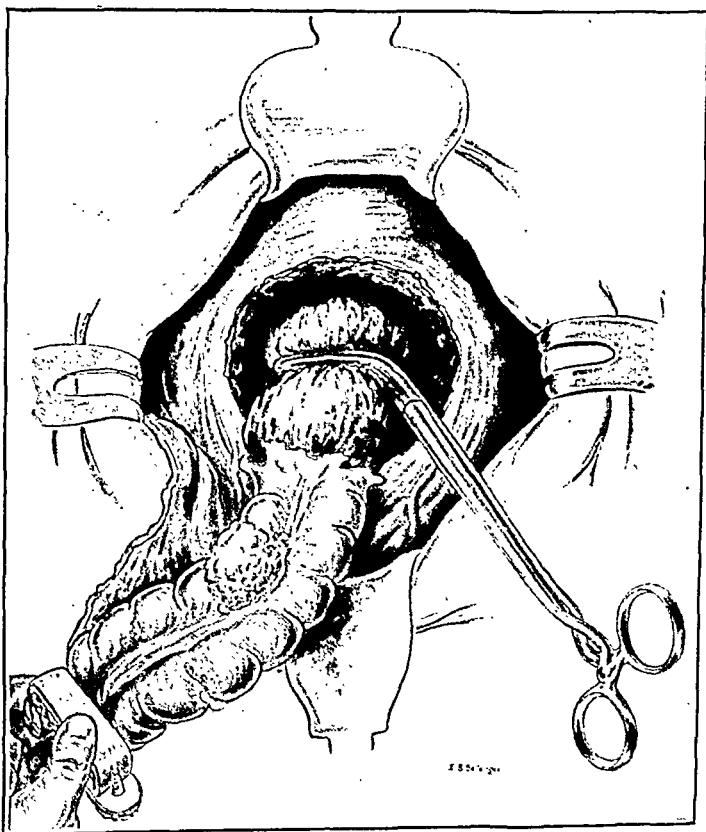


Fig. 19.—The lower end of the rectosigmoid segment is closed by a Wertheim's vaginal clamp before the rectum is divided.

point has been reached, a few figure-of-eight sutures are inserted from the external surface of the bowel in order to complete the anastomosis. (See inset Fig. 20.) Only one layer of sutures is used. The sutures are inserted from the lumen of the bowel, because on account of the cramped position it is most difficult to place the posterior layer of sutures in position from the external surface.

A long needle-holder is used to insert the sutures, and another one in the left hand serves to pick them up. By employing this double needle-holder device, it is surprising to see how deep down in the pelvis an anastomosis can be made. The pelvic peritoneum is sutured over the

anastomosis. A tube is introduced through the abdominal wound down to the anastomosis and another one is inserted through the rectum. The sphincter is divided.

About six or seven days after the operation, it will often be found that if saline solution be injected through the anus, some of it will come out of the abdominal tube. This is owing to the fact that a leak has developed in the anastomosis. The tube (or a smaller one) is therefore left in position until such time as fluid injected through the rectum shows that the anastomosis has healed. About two weeks after this, the spur of the anus is crushed.

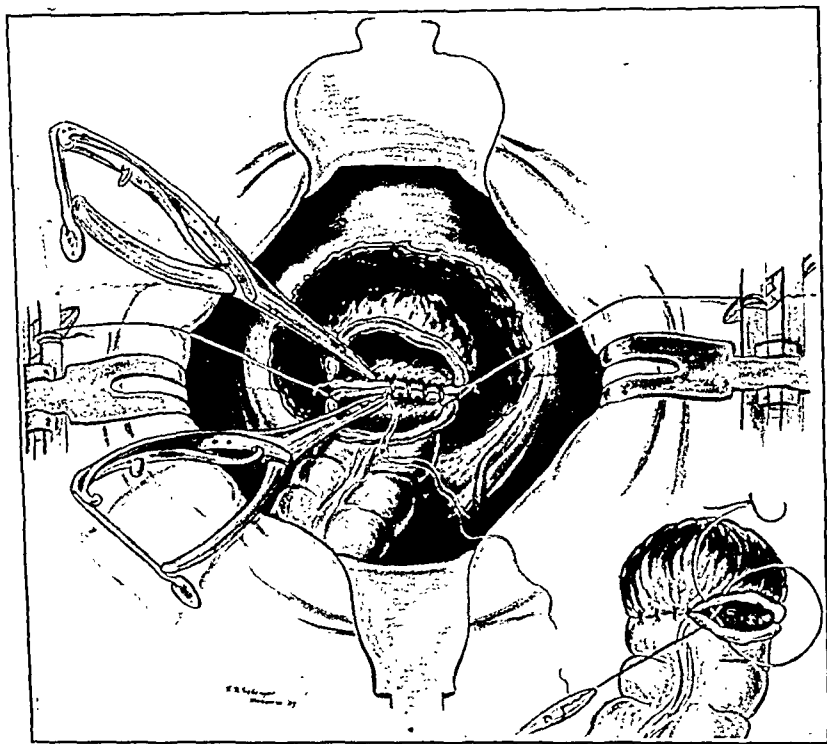


Fig. 20.—Shows, semidiagrammatically, sutures being inserted from the mucous membrane inside the bowel, so as to join the posterior wall of the divided end of the sigmoid with that of the divided end of the rectum. It also shows the use of the two needle-holders, which enable the suturing to be done in the depths of the pelvis, and how the anastomosis is guy-roped to the frame, so that in such a deep wound the ends are kept in accurate position and exact suturing is made possible. The inset shows figure-of-eight sutures being used to coapt a small section of the anterior edges of the rectum and colon segments.

As the rectum is very wide, where it is divided, and as the cut end of the sigmoid can be widened by a vertical cut, the anastomosis is rather easier to make than would be expected.

A sutured rectosigmoid anastomosis is particularly applicable after rectosigmoid resection for a diverticular tumor.

*“Telescopic” Rectosigmoid Anastomosis.*—In some cases of rectosigmoid resection, a sutured anastomosis between the sigmoid and the



stump of the rectum cannot be made because of mechanical disabilities. This happens in fat people, in males with narrow pelves, in the case of a small or short rectal stump. In circumstances such as these, the rectal stump may be closed as shown in Fig. 21, the peritoneum sutured over it, and the divided end of the sigmoid implanted into the abdominal wall. Then at a later stage, when the peritoneum has become "glued" on to the rectum (Fig. 22), the sigmoid may be disconnected and drawn through an opening, which is made in this rectal pouch, the sphincter of which is divided. Fig. 23 shows diagrammatically the cut end of the sigmoid

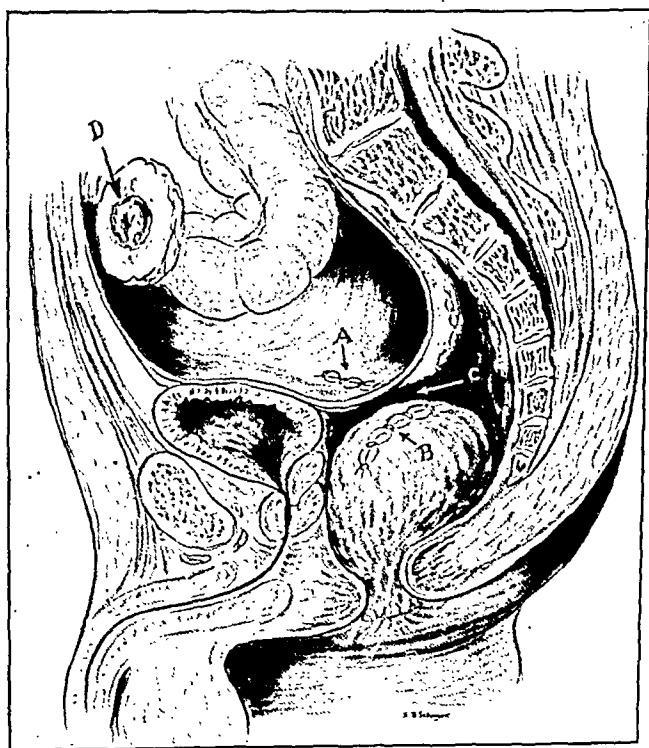


Fig. 21.—Closure of the rectal stump after a rectosigmoid resection. *A*, the sutures closing the peritoneum over it; *B*, the sutures closing the stump of the rectum; *C*, the subperitoneal space left between the sutured stump and the peritoneum; *D*, is the anus.

telescoped into the rectal pouch. A few sutures connect the peritoneum of the sigmoid to the peritoneum covering the rectal pouch, so that, as the sigmoid is drawn down, peritoneal surface becomes applied to peritoneal surface. A slotted tube (*B*), fixed in position with a safety pin, is used to keep the anastomosis in position and to drain the rectal pouch.

As the sigmoid is functionless and the rectum patulous from the division of the sphincter ani, there is no more danger from this "telescopic" operation than from drawing the sigmoid on to the surface of the abdominal wall to make an ordinary abdominal artificial anus.

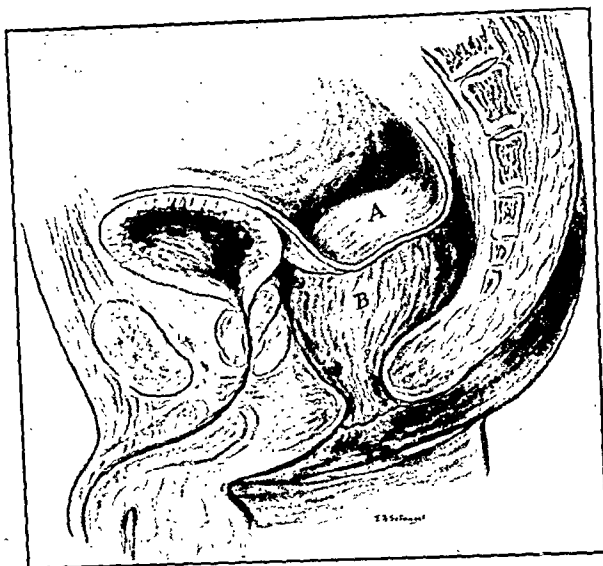


Fig. 22.—Diagrammatic (sectional) representation of the condition a month later. The peritoneum (A) is now shown adherent to the rectal stump (B) and there is no peritoneal space to admit of dangerous spreading subperitoneal cellulitis.



Fig. 23.—Shows diagrammatically the cut end of the sigmoid telescoped into the rectal pouch. A few sutures connect the peritoneum of the sigmoid to the peritoneum covering the rectal pouch, so that, as the sigmoid is drawn down, peritoneal surface becomes applied to peritoneal surface. A indicates ring of skin around artificial anus sutured to rubber tube; B, slotted tube fixed in position with a safety pin, used to keep the anastomosis in position and to drain the rectal pouch; C, gauze and safety pin preventing the tube from going up.

A difficulty, however, in this method is that, sometimes, it is difficult to make the opening in the rectal pouch, because the bladder falls over and adheres to the rectal stump.

The method is particularly applicable to bad cases of carcinoma of the lower end of the sigmoid; for the making of the telescopic anastomosis can be delayed for six or twelve months, when the patient will have greatly improved in health as a result of the removal of the malignant growth and when the circulation of the rectal stump—which is sometimes disturbed in these cases—will have improved.

#### CASE HISTORIES TO SHOW VALUE OF SUTURED RECTOSIGMOID ANASTOMOSIS ON DEFUNCTED COLON

**CASE 1.**—An old and very debilitated man with carcinoma of the lower end of the sigmoid, acute intestinal obstruction, and a late stage of diabetes. *Stage 1.*—Disconnecting anus in the proximal transverse colon. *Stage 2.*—Rectosigmoid resection with closure of the rectal stump and implantation of lower cut end of sigmoid into loin. *Stage 3.*—Six months later—resection of sigmoid mucous-fistula (artificial anus) and anastomosis by suture of lower end of sigmoid with rectal stump. Recovery: lived three years.

**CASE 2.**—Female, aged fifty years; diverticular tumor, intestinal obstruction. *Stage 1.*—Disconnecting anus in the distal part of transverse colon and exploration of the abdomen. Large adherent mass filling the whole of the pelvis. Regarded as an inoperable carcinoma of the sigmoid. *Stage 2.*—Three months later, at a second operation, further scrutiny of the mass now gave the impression that it was an inflammatory diverticular tumor, and not a carcinoma, as at first thought; but it was, however, still irremovable. *Stage 3.*—Six months later, at a third operation, it was found that, as the result of six months defunctioning of the distal colon, the tumor of the sigmoid had become so much smaller and less adherent that it now appeared possible to remove it; and the whole of the lower two-thirds of the sigmoid, which was involved in the tumor mass and widely adherent to adjacent structures, was removed. The severed end of the sigmoid was anastomosed to the upper part of the rectum. The patient recovered with complete function. Fig. 24 is an x-ray, made six months after the operation, of a barium clysma in this patient.

**CASE 3.**—Patient, aged seventy-five years, male, greatly debilitated, carcinoma of the lower end of the sigmoid, acute intestinal obstruction with great distention. *Stage 1.*—A disconnecting anus was made at the hepatic flexure (the transverse colon was short owing to the great distention), a loop being made by suturing the proximal limb of the transverse colon to the ascending colon. Exploration revealed the fact that the patient had a sigmoid growth, which, because it was adherent to the surrounding structures including the bladder, appeared to be inoperable. Two weeks later, the patient developed complete prostatic obstruction and became uremic. *Stage 2.*—Cystotomy: the bladder was connected to a continuous suction apparatus. *Stage 3.*—Some time later: prostatectomy. *Stage 4.*—Four months later: Exploration showed a small contracted distal colon and the growth now lying quite free, except for a slight attachment to the bladder, and apparently quite operable. A rectosigmoid resection was carried out and an immediate single layer sutured anastomosis made, the union being between the upper third of the rectum and the lower end of the upper third of the sigmoid. Notwithstanding the patient's great weakness and long illness, this operation did not disturb his general condition in the slightest or the function of his colostomy. He recovered from the effects of the operation, but died two months later.

These cases, illustrating as they do, the most difficult surgical problem involved in carcinomas or in diverticular tumors of the lower end of the sigmoid and the rectosigmoid junction, show the particular application of the abdominorectosigmoid resection method. They also show the lenity of the operation, since it was employed in the these very old and very sick people.



Fig. 24.—X-ray of a case in which a diverticular tumor involving most of the sigmoid was removed, and the divided end of the sigmoid anastomosed to the upper part of the rectum. (From Brit. J. Surg.)

#### CASE HISTORIES TO ILLUSTRATE TELESCOPIC METHOD OF RECTOSIGMOID ANASTOMOSIS

The two following brief case histories—Cases A and B—illustrate the uses of this telescopic method of rectosigmoid anastomosis:

CASE A.—A very fat man, aged fifty-six years, a hotel keeper, developed acute intestinal obstruction. He was operated on in the country, and what appeared to be an inoperable carcinoma of the sigmoid was found. In order to relieve the obstruction, an artificial anus was made in the upper end of the sigmoid.

Subsequent investigation by me created the suspicion that the tumor was inflammatory and that it was the result of an extensive diverticulitis.

At a second operation, the whole of the sigmoid, including the portion bearing the artificial anus, was removed. It was impossible to approximate the divided ends of the bowel and therefore to make an anastomosis. Consequently it was necessary to close the divided rectum by suturing separately the muscle layer and the peritoneum (shown in Fig. 21) and also to implant the distal cut end of the beginning of the sigmoid into the loin, where it would function as an artificial anus.



Fig. 25.—Skiagram of the descending colon and the rectal stump in this case. After four years the distal end of the descending colon had elongated a little from the increased function imposed on it. Note the smallness of the rectal stump. 1 is the lower end of descending colon; 2, the stump of rectum. (From Australian & New Zealand J. Surg.)

Four years later, at the request of the patient, who could not any longer tolerate the artificial anus, I decided to make an attempt to unite the descending colon to the rectum. The skiagram (Fig. 25) shows the level of the division of the sigmoid—almost at its beginning—and the smallness of the rectal stump.

After making a disconnecting anus in the manner already described and preparing the distal colon, the sigmoid was joined to the rectal stump by a telescopic anastomosis made in the way which has been described (Fig. 23).

The following are the detailed steps of the operation: (a) The abdomen was opened by a median subumbilical incision; (b) an incision was so made round the artificial anus that a substantial ring of skin was left attached to the mucous membrane; the anus was then disconnected from the abdominal wall and the descending colon extensively mobilized; (c) a rubber tube 2.5 cm. (1 inch) in diameter, cut as shown in Fig. 23 was now sutured to the ring of skin which had been left attached to the artificial anus for this purpose. (d) A sponge holder with a swab on the end was now introduced through the anus into the rectum and pressed against its upper blind end. An incision 3.75 cm. ( $1\frac{1}{2}$  inches) long was made through the rectal wall. The forceps was now made to grip the end of the tube and draw it, with the attached bowel, through into the rectum.



Fig. 26.—An x-ray picture of the rectum of this patient, made after a barium clyisma followed by injection of air. It was taken four years after the "telescopic" operation. Note the straight tubelike rectocolic segment. (From Brit. J. Surg.)

The rectal stump had contracted from disuse, and, as the patient was very fat, a tunnel had therefore to be made posteriorly to the bladder before the rectum could be incised. Consequently, when the bowel was drawn through this tunnel, there was no space whatever which would permit the manipulations required for the insertion of sutures in order to unite the cut edge of the rectal wall to that of the colon. Union of the bowel ends was then attained as follows: (e) The obliquely cut part of the tube was drawn down through the anus and kept in this position by means of gauze and a very large safety pin inserted as shown in Fig. 23. The sphincter grasping the obliquely cut part of the tube prevented the tube from

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## ACUTE CHOLECYSTITIS

PROBLEMS CREATED BY AN ATTEMPT TO CORRELATE ITS CLINICAL,  
SURGICAL, AND PATHOLOGIC MANIFESTATIONS

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IN 1928, H. O. Bruggeman concluded a paper, in which were quoted the views of the leading surgeons of this and other countries with regard to the treatment of acute cholecystitis, with the following statement: "I wish to express the hope that some day surgeons will be fairly unanimous in their views on the treatment of acute inflammation of the gallbladder." That hope is, if anything, further from fulfillment today than it was at that time.

It is not the purpose of this paper, however, to express a dogmatic opinion in regard to this highly controversial subject, nor to argue the case for immediate, early, or delayed operative treatment of acute cholecystic disease. Our purpose is to consider some of the problems created by an attempt to correlate the clinical, surgical, and pathologic manifestations of the disease, and, since at present there is no uniformity of opinion among surgeons as to what constitutes immediate, early, or delayed treatment, to raise the question whether there ever can be, because of the nature of the disease.

The advocates of each of these schools seem to stand firm in the belief that theirs is the proper method of treatment, and furthermore each group believes there is good evidence to substantiate its arguments. As a consequence, confusion has increased. "Immediate," for example, may mean that operation was performed within a few hours after the onset of the attack of cholecystitis. In such cases the patient is admitted to a hospital and is immediately operated upon. Indeed, patients with acute cholecystitis are sometimes subjected to an exploratory operation in the incipient stages of the disease because the condition has been mistaken for ruptured ulcer or acute appendicitis. Protagonists of this school claim that these patients as a group do well. As a rule, they are operated on when they are still in good general condition, before they become dehydrated from prolonged vomiting or anorexia, and while the acute process is localized to the site of origin and before it involves the pericholecystic tissues and biliary passages. At this time, too, one is not so often called on to combat hemorrhage from friable, edematous, or indurated structures,

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moving downward. The safety pin prevented it from going upward. The bowel ends were therefore held in position in which they were placed. The slotted part of the tube drained any contents which might have accumulated in the rectal cavity. A drainage tube was introduced abdominally down to the junction of the colon with the rectum.

The convalescence of the patient was uneventful. Four weeks after the operation, when it was found that the anastomosis was firmly healed, a little local anesthetic was injected into the small strip of skin between the bowel ends and the spur of the midcolic anus was crushed. The artificial anus then closed naturally in a very short time. Four years later, an x-ray (Fig. 26) showed that this patient was functioning perfectly and that no contraction had taken place at the telescopic union.

**CASE B.**—A female, aged fifty-five years, who had a carcinoma of the lower end of the sigmoid, was operated on in the following stages: *Stage 1.*—Disconnecting anus made at the proximal part of the transverse colon, when an exploration revealed a carcinoma situated close to the lower end of the sigmoid.

*Stage 2.*—Three weeks later: Resection of the lower end of the sigmoid and the upper part of the rectum, closure of the rectum, and implantation of the cut end of the sigmoid into the abdominal wall. *Stage 3.*—Many months later when the patient was in good health: mobilization of the upper part of the sigmoid and the descending colon, and the making of a telescopic anastomosis with the rectal pouch, the sphincter ani of which was divided. This patient is now well and has functioned normally for sixteen months.

#### RESULTS

The case histories quoted are only a few examples out of many of the type of cases in which, with no other method, I could achieve the same results. So far, the series of patients on whom I have operated by the defunctioning method is not yet extensive enough to make generalizations. The immediate results in the patients on whom I have operated by this method, however, even in the most difficult cases, have been so successful and show so clearly the great potentialities of operating by this principle, that surgery of the distal colon has no longer, for me, the anxiety that it formerly held.

In cases in which a sutured anastomosis was made on the "defunctioned" colon, the convalescence of the patients was remarkably quiet and the abdominal cavity manifested no reaction of any sort. In one operation which involved the removal of a large carcinoma of the transverse colon adhering to an abdominal scar and also that of a segment of small intestine, the subsequent convalescence was so smooth and so free from reaction that one could not but be struck with the very great advantage of these operations on the "defunctioned" colon.

I have been able to unite the sigmoid to the rectum in a very debilitated patient who suffered from diabetes, and who came into hospital with acute intestinal obstruction; to join up, under very adverse circumstances, the upper part of the sigmoid to the lower two-thirds of the rectum—and without using a single suture; to remove growths of the sigmoid which at the first approach were inoperable; and to slit up the sigmoid and remove single and multiple adenoma. I feel, therefore, that a method of operating, which has such potentiality for cure in the bad cases, is a method which might well be the surgeon's choice for routine colon surgery.

present, the presence or absence of stones, the number of previous attacks, general and local tissue resistance, and the acuteness and degree of the interference with the blood supply to the gallbladder. It is well known that after the acute clinical signs in the right upper abdominal quadrant have subsided, and when the pulse rate and temperature have returned to normal, the operative and histologic picture may remain that of acute cholecystitis. In fact, one of the most interesting features of biliary disease, as W. J. Mayo has so frequently pointed out, is the impossibility in many instances of correlating the clinical picture with the degree of inflammation in the gallbladder. It is therefore conceivable that the results of operation reported for a series of cases in which a definite pathologic diagnosis of acute cholecystitis has been made might be radically different from those reported for a group of cases in which the clinical signs and symptoms alone have been the basis of the diagnosis.

Is the diagnosis of disease of the gallbladder to be based on the clinical, surgical, or pathologic findings? In few other diseases are the clinical and the pathologic diagnoses so likely to be at variance. This fact has been emphasized also by Andrews, Heuer, and others. Cases in which a clinical diagnosis of acute cholecystitis has been made may fail to show evidence of the acute process on pathologic examination; and, conversely, cases in which inflammation in the gallbladder is considered from a clinical standpoint to be chronic not infrequently give evidence of acute or subacute disease histologically. How often does this occur? In an effort to clarify our own thought on these questions, we have reviewed the recent literature on the treatment of acute cholecystitis and have examined the histories in a consecutive series of cases of cholecystitis of all types in an effort to correlate the clinical, surgical, and pathologic findings.

A group of 200 consecutive cases of cholecystic disease of all types, in which cholecystectomy was performed and microscopic sections were studied by Dr. A. C. Broders, was used as the basis for the following studies. The clinical, surgical, and pathologic diagnoses were noted in all cases (Table I). In 176 cases, for example, a clinical diagnosis of chronic cholecystitis had been made, but only 129 (73.3 per cent) of these cases were classified as being chronic cholecystitis by the surgeon at the time of operation. In 46 of these cases (26.1 per cent) the surgical diagnosis was subacute cholecystitis and 1 case (0.6 per cent) was called acute cholecystitis. The pathologist, after gross and microscopic inspection, corroborated the diagnosis of chronic cholecystitis in only 100 cases (56.8 per cent). In 72 cases (40.9 per cent) the condition was found by him to be subacute cholecystitis superimposed on a chronic cholecystitis, and in 4 cases (2.2 per cent) he found acute cholecystitis to be present. The remaining data are given in Table I.

with possible injury to the common duct or the hepatic blood supply. The good results said to have been obtained in such cases and the low morbidity and mortality recorded have undoubtedly brought about the recent wave of enthusiasm for "immediate" operation in cases of acute cholecystitis.

"Immediate" operation, however, is also applied not only to cases in which patients are operated on soon after their arrival in a hospital, but also to cases in which such patients may have suffered an attack of acute cholecystitis for several days before admission. Usually these are cases in which the patient has been guilty of procrastination, or in which the original attending physician has instituted conservative treatment as a primary procedure. Such patients are, as a rule, in poor condition for operation and the technical difficulties are increased at the time of surgical intervention. It is operations in this type of case which cause the advocates of "delayed" treatment to view with some apprehension the teaching of those who advise prompt surgical intervention. For example, Zinninger reported the results obtained by "immediate" (on the patient's admission to the hospital) operation in 35 cases. In 12 of these cases the duration of the attack was less than forty-eight hours. There were no deaths in the group. In 15 cases the attack had lasted for from two to five days. One of these patients died, giving a mortality of 6.6 per cent. In 8 cases immediate operation was performed after the patient had been sick for five or more days at home. Of these patients 2 died, or a mortality of 25 per cent. While this series is small, at least it shows a trend of possible significance.

Confusion is also caused by the fact that authors speak of "early" operation without a uniform definition as to what they consider early to be. To one, "early" may mean operation within thirty-six hours after the onset of the attack; to another it signifies operation within five days of the onset of acute symptoms; and to a third, cases in which operation is performed at a later period may still fulfill the requirements of early operation. On the other hand, at least one defender of the "delayed" treatment of acute cholecystitis said that he believed that the best policy was to hospitalize the patient for two, three, or four days, or longer, after the onset of the attack before surgical intervention was contemplated, depending on the clinical picture present in the individual case. It seems reasonable to believe, therefore, that there is some duplication of material among those who are advocating "early" and "delayed" treatment.

There are so many variable factors involved in a consideration of acute cholecystitis that it is frequently difficult to tell not only the time of onset of the acute attack, but also the duration of the acute phase. These variables may include, among many others, the presence or absence of an infecting organism and its virulence if one is

## COMMENT

The question that obviously suggests itself is whether there can ever be any uniformity in the treatment of acute cholecystitis, and furthermore, if such uniformity is desirable? Is there necessarily only one way for all surgeons to treat all patients with acute cholecystitis? Can so complicated a disease be reduced to such simple terms as "hours after onset," or "delayed," "early," or "immediate" operation? In view of the many variable factors that may complicate the individual case, it hardly seems reasonable to believe that it can.

We have attempted to show the difficulties and uncertainties of accurate clinical diagnosis. In the final analysis, however, it appears that no rule of thumb can ever substitute efficiently and effectively for sound surgical judgment in the management of the individual case in which there is an acute inflammatory process in the gallbladder.

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These figures serve to emphasize the frequent difficulty of accurate clinical diagnosis of the degree of inflammation present in the individual case of cholecystitis.

TABLE 1

CORRELATION OF CLINICAL, SURGICAL, AND PATHOLOGIC DIAGNOSIS IN 200 CASES OF DISEASE OF THE GALLBLADDER

CLINICAL DIAGNOSIS	CASES	SURGICAL DIAGNOSIS						PATHOLOGIC DIAGNOSIS					
		CHRONIC CHOLE- CYSTITIS		SUBACUTE CHOLE- CYSTITIS		ACUTE CHOLE- CYSTITIS		CHRONIC CHOLE- CYSTITIS		SUBACUTE CHOLE- CYSTITIS		ACUTE CHOLE- CYSTITIS	
		CASES	PERCENTAGE	CASES	PERCENTAGE	CASES	PERCENTAGE	CASES	PERCENTAGE	CASES	PERCENTAGE	CASES	PERCENTAGE
Chronic cholecystitis	176*	129	73.3	46	26.1	1	0.6	100	56.8	72	40.9	4	2.3
Subacute cholecystitis	17	3	17.7	10	58.8	4	23.5	3	17.6	13	76.5	1	5.9
Acute cholecystitis	6	0	0	4	66.7	2	33.3	1	16.7	4	66.6	1	16.7

\*In 1 additional case primary carcinoma of the gallbladder was present.

In the majority of cases the total leucocyte count is an unreliable aid in determining the degree of inflammatory reaction present in cholecystic disease. The presence of residual, localized, right upper quadrant tenderness of even a slight degree, however, should lead one to suspect that subacute cholecystitis may be present, although our studies indicate that this sign is also unreliable; when present, its interpretation is rendered difficult by the variation in the reaction of individuals to pain.

In 174 of the 200 cases in this group the Graham-Cole test was performed. The gallbladder was shown roentgenographically to be poorly functioning or to be nonfunctioning in 71.8 per cent of these cases. The test, however, was of little value in distinguishing the chronically from the subacutely, inflamed gallbladder. However, in the 5 cases of pathologically acute cholecystitis in which the dye excretion test was carried out, in not one was there normal function.

Bannick has recently emphasized the value of the blood sedimentation rate in following the progress of cases of acute cholecystitis. For those who desire to wait until the acute process has subsided before operating, it would appear to be a more sensitive index than the total leucocyte count, the pulse rate and temperature, or the degree of tenderness. Furthermore, failure of the sedimentation rate to return to normal after a proper trial of conservative management may indicate impending rupture or gangrene of the gallbladder and the necessity for surgical intervention.

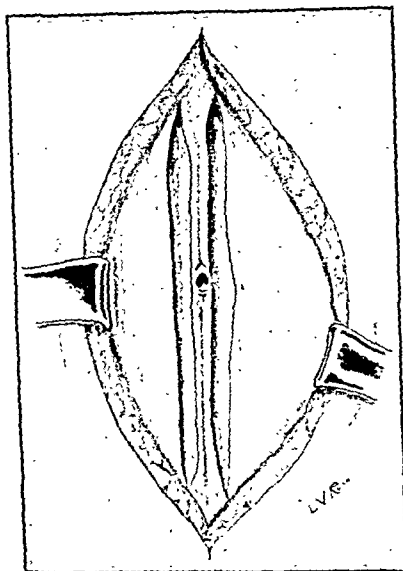


Fig. 2.

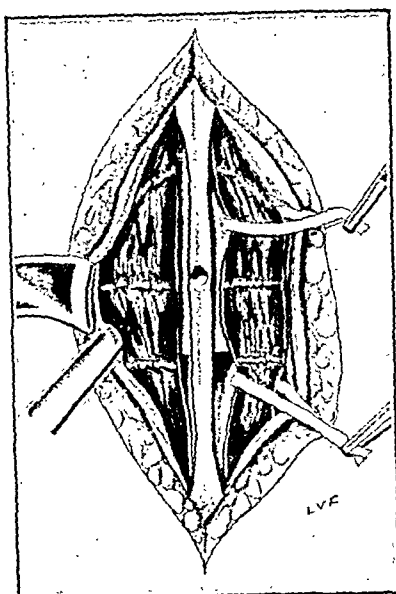


Fig. 3.

Fig. 2.—The umbilicus has been excised and the sheaths of both rectus muscles opened near the midline.

Fig. 3.—The left rectus muscle has been freed and is surrounded by loops of beef fascia. The right rectus muscle is being freed by blunt dissection.

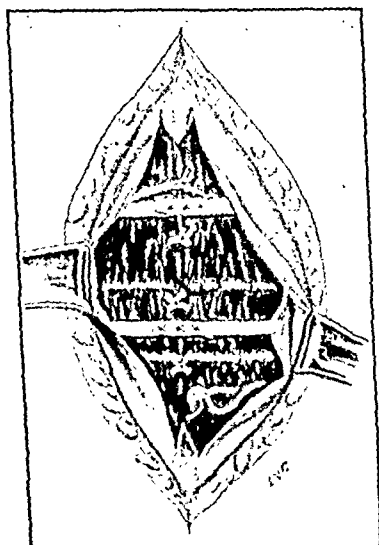


FIG. 4.

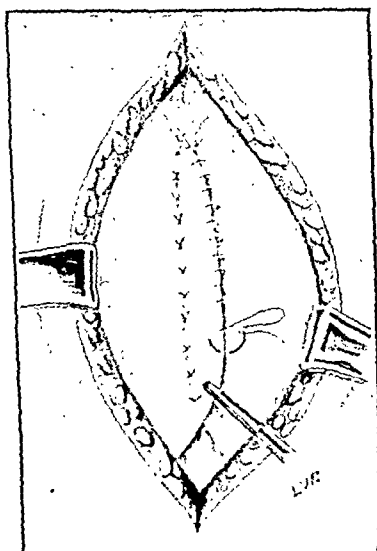


Fig. 5.

Fig. 4.—The fascia loops have been sutured on the anterior surface of the muscles retaining them in their new position without tension. The medial borders of the muscles have been approximated with interrupted No. 0 chromic sutures.

Fig. 5.—Interrupted mattress sutures of No. 1 chromic catgut have been placed, the fascia is overlapped with running sutures of No. 0 chromic catgut.

## A RECONSTRUCTION OPERATION FOR DIASTASIS RECTI

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(From the Rush Infirmary Clinic)

A SATISFACTORY technique for the reconstruction of the abdominal wall in diastasis recti provides for the transplantation of the rectus muscles to the midline with minimum injury to the nerve or blood supply, satisfactory fixation of the muscles in this position, narrowing of the rectus sheaths, and adequate strengthening of the fascia in the intermuscular area. The method described below satisfactorily meets these requirements.

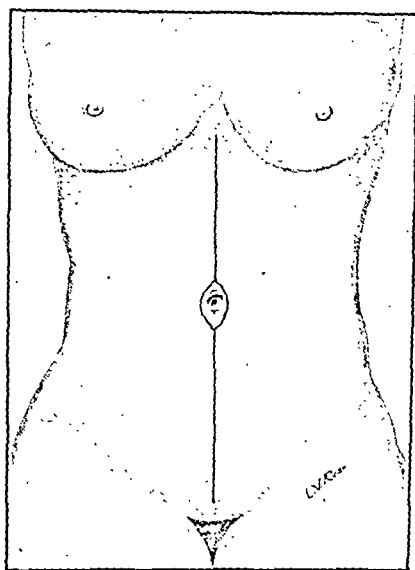


Fig. 1.—The incision.

### TECHNIQUE OF THE OPERATION

A midline abdominal incision is made, beginning at the xiphoid process and extending downward to the symphysis pubis, excising the umbilicus (Fig. 1).

The anterior sheath of each rectus muscle is opened in its entire length at the medial border, resulting in two parallel incisions just lateral to the linea alba (Fig. 2). The fascia of the anterior sheaths is dissected laterally on either side and the rectus muscles gently freed from their beds by blunt dissection, care being exercised to protect the nerves and blood vessels.

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## OSTEODYSTROPHY OF UNKNOWN ETIOLOGY\*

### CASE REPORT

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University of Chicago)*

CASES of multiple and progressive deformities of the skeleton which do not fit into any of the recognized classifications of skeletal dystrophies are only occasionally seen. The following case of idiopathic osteodystrophy has been under observation at the University of Chicago Clinics for nine years and both the deformities and the resultant disabilities have progressed in spite of medical therapy and repeated attempts at correction by means of surgical operations.

A. K., male, aged fifteen years, was first admitted to the University of Chicago Clinics, Oct. 8, 1928, at the age of six years and eleven months, because of multiple progressive deformities and increasing difficulty in walking. He was the first-born child of parents who were first cousins. Delivery was completed with forceps after a labor that lasted for twenty-seven hours. No abnormalities were noted at the time of birth, but a few days later the mother found a small hard lump on the cranium just in front of the posterior fontanel. He was able to sit up at the age of nine months and never crawled on his hands and knees, but "scooted" along on his buttocks until he began to walk at sixteen months. From the time that he began to talk his voice was observed to be raspy and hoarse. At eighteen months of age, the valgum deformity of his knees was noted, and without a definite diagnosis he was treated with cod liver oil, phosphorus, and Fowler's solution. There was also a soft pea-sized tumor of the skin of the lower lip, a large soft tumor beneath the skin of the left flank, and a one-half by one inch-sized pigmented spot on the skin of the left side of the neck.

A bilateral tibial osteotomy was performed at the age of two years, but when weight-bearing was resumed the valgum deformity of the knees recurred. An examination at this time revealed partial occlusion of the bony canal of the left ear caused by a small exostosis with slight diminution of hearing. When he was aged about three years, curvature of the spine and a bony growth on the plantar aspect of the left calcaneus were observed. An attempt to correct the scoliosis and to straighten the legs by operation was not successful.

\*This study was conducted in part by a grant from the Douglas Smith Foundation for Medical Research.

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At a point about two inches above the umbilicus level, a strip of beef fascia is passed transversely behind the left rectus muscle and a loop formed which is held by an artery forceps. This same procedure is repeated at a point about one and one-half inches below the umbilicus. (Fig. 3.) The medial end of each strip of beef fascia is then carried transversely to the right, anterior to the linea alba and posterior to the right rectus muscle.

The rectus muscles are approximated and sutured to each other in the midline by interrupted sutures of No. 0 chromic catgut. The ends of the respective strips of beef fascia are brought over the anterior surfaces of the muscles and sutured to each other with No. 0 chromic catgut, thus forming a loop to retain the muscles in their new position. (Fig. 4.) It is important that the loops be brought together not tightly enough to constrict the muscle. The anterior sheaths of the recti are then overlapped in the midline by interrupted mattress sutures of No. 1 chromic catgut. A continuous suture of No. 0 chromic catgut fixes the free border of the fascia. (Fig. 5.) The skin is closed with figure-of-eight silkworm stitches.

#### AFTER-TREATMENT

The patient is kept in bed for three weeks after the operation. Muscular exertion is avoided for two months. An abdominal support may be employed very wisely for several weeks after getting out of bed. After this period exercises are recommended, not only for the strengthening effect, but also to encourage a compensatory thickening of the abdominal fascia. A protuberant abdomen may result from the prolonged use of an abdominal girdle or support, due to atrophy of nonuse.

#### SUMMARY

An operation is described for the repair of diastasis of the rectus abdominis muscles.

1. A long midline incision is made and the umbilicus excised.
2. The muscles are dissected from their beds and retained in the midline by loops of beef fascia.
3. The muscles are approximated in the midline by interrupted sutures.
4. The fascia of the anterior sheaths of the rectus muscles is overlapped in the midline.
5. After-treatment consists of three weeks' rest in bed and use of an abdominal support for six weeks followed by active exercise.

The past medical history of the patient was negative. He had complained of difficulty in swallowing and seemed to have more trouble with liquids than with solid foods. There was occasional nausea and emesis sometimes occurred immediately after eating, but no organic basis for this could be established.

The family history revealed no other instance of any type of congenital abnormality or developmental deformity. The one other child, a younger brother of the patient, is now twelve years of age, well developed and normal in every respect.

*Physical Examination.*—At the time of his first admission to the Clinics, physical examination showed a slender, maldeveloped white male who appeared to be older than the stated age of seven years. Both trunk and extremities were long and angular, with gross deformity of the calvarium, spine, thorax and lower extremities. (Fig. 14.) The abnormal findings at this time may be itemized as follows:

Oct. 8, 1928:

1. Asymmetry of the face.
2. Three small bony prominences (exostoses) along the parietal occipital suture line and a fourth over the lateral margin of the left orbit.
3. Small raised tumor on the sclera of the left eye at about the five o'clock position.
4. Small, soft, pea-sized subcutaneous tumor on the lower lip.
5. Small bony growth on the mandible below and lateral to the left lateral incisor.
6. Hearing in the left ear slightly diminished and a small exostosis partially occluding the external canal.
7. Palpable exostoses on the right transverse processes of the fifth and sixth cervical vertebrae.
8. Loss of normal cervical curve and loss of motion in cervical spine.
9. Brown pigmentation of the skin area 1.5 by 3.5 cm. on the anterolateral surface of the left side of the neck. A similar, but smaller area of pigmentation was present over the back of the left scapula.
10. Flat chest; pot belly; beading of the ribs at costochondral junctions.
11. Marked scoliosis of the spine and deformity of the sacrum.

TABLE I

DATE	BLOOD SERUM				PRODUCT OF Ca AND P
	CALCIUM	PHOSPHORUS	CO <sub>2</sub> CONTENT	PH	
1929	MG. PERCENTAGE	MG. PERCENTAGE	VOL. PERCENTAGE		
Aug. 17	11.70	4.85	59.30	7.61	56.8
Aug. 20		5.71	61.8	7.57	
Aug. 22		5.924	69.4	7.55	
Aug. 26	11.6	4.76	57.2		55.4
Aug. 28	12.21	5.51	63.8	7.57	67.4
DATE	URINE			REMARKS	
	VOL. 24 HOUR	SPECIFIC GRAVITY	CALCIUM	MG. PER 24 HOURS	
Aug. 22	700 c.c.	1.020	105.7	On Ca balance diet Regular hospital diet	
Aug. 27	590 c.c.	1.022	91.76		

When he was five years of age, a soft tissue tumor was observed on the sclera of the left eye at about the five o'clock position and a bony exostosis in the left supraorbital rim was noted. In January, 1928, when he was six years of age, he began to have pain in the left lower abdomen. This had recurred at intervals and was thought to have been caused by the scoliosis and vertebral exostoses. After a period of head and foot traction, osteotomies were again performed and oral administration of calcium salts was begun in addition to the cod liver oil, which had been continued since infancy.

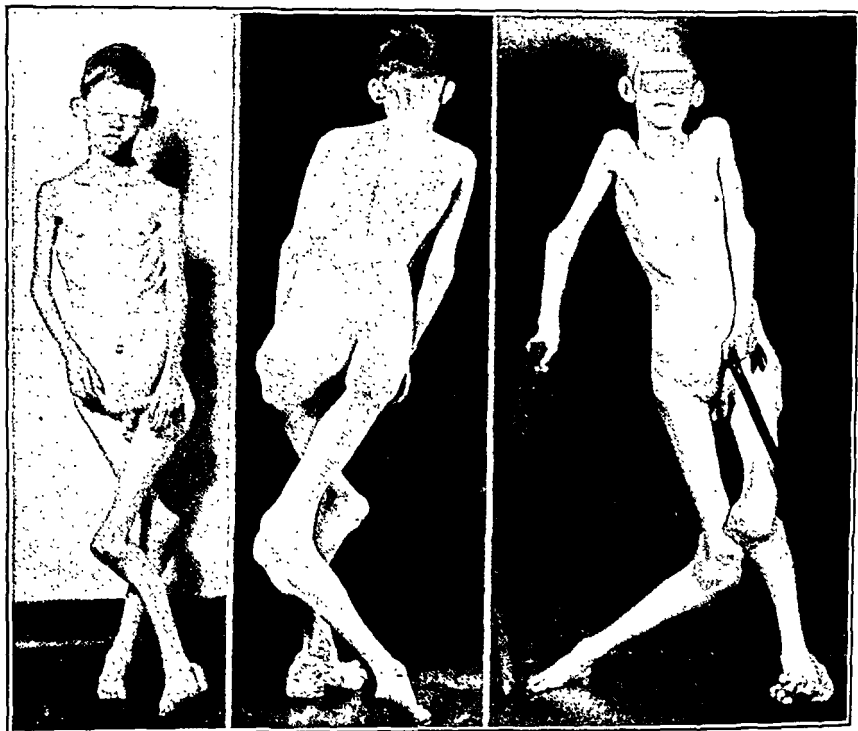


Fig. 1A.

Fig. 1B.

Fig. 1C.

Fig. 1A.—Appearance of the patient on admission, aged six years eleven months. The marked deformity of the lower extremities, multiple exostoses, and the rachitic rosary are shown. The apparent asymmetry in the length of the arms is caused by the scoliosis. The large lipoma of the left flank is not apparent in this photograph.

Fig. 1B.—May 9, 1931, aged nine years. All deformities have increased. The osseous growths on tibia, femur, pelvis, spine, and ribs and the bony tumor of the left calcaneus have grown larger.

Fig. 1C.—Dec. 21, 1935, aged thirteen years.

At the time of his first admission to the University of Chicago Clinics, aged six years and eleven months, his parents stated that all of the deformities had progressed in spite of the repeated osteotomies and attempts at correction. The bony growth on the plantar surface of the left foot had enlarged so that a shoe one and one-half sizes larger than the right was necessary. This mass caused some pain and made walking more difficult.

In August, 1929 (Table I), analyses of the blood serum showed normal calcium, phosphorus, and carbon dioxide with a slight shift of the hydrogen ion content toward the alkaline side. The excretion of calcium and phosphorus in the urine was also found to be within normal limits. These determinations have been repeated at subsequent admissions but have never been found to be abnormal.

*Roentgenographic Examinations.*—These have been made at intervals during the past seven years and have revealed progressive enlargement of the previously described bony excrescences and exostoses.

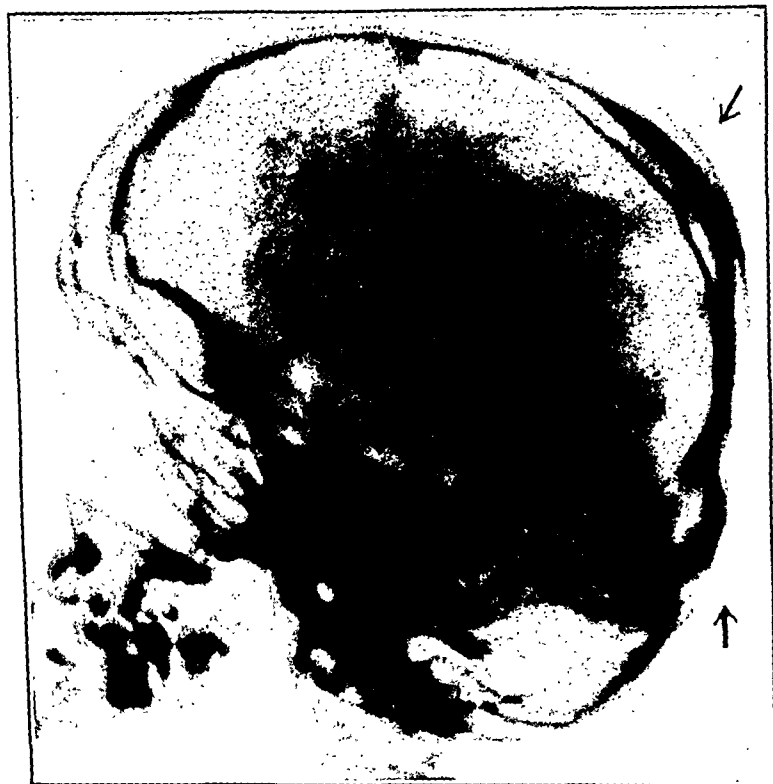


Fig. 2B.—Roentgenogram, Dec. 21, 1935, at the age of thirteen years. The osteomas of the calvarium show characteristic decrease in size and density.

The skull (Fig. 2) showed smoothly rounded osseous growths 1 to 2 cm. in diameter on the outer table of the calvarium in the left parietal and occipital regions; there were no visible changes on the inner table.

The spine (Fig. 3) showed a marked double-curved scoliosis, with small exostoses from the transverse processes of the fifth and sixth cervical vertebrae and wedging of the lumbar vertebral bodies.

Roentgenographic examination of the pelvis (Fig. 4) showed gross deformity of the pelvic bones. The outlet was narrowed and compressed to the left side. Irregular bony excrescences were present on the ilium above each acetabulum. The head and neck of each femur showed cortical thinning with progressively enlarging exostoses on the greater trochanters.

12. Soft, freely movable subcutaneous tumor in the left flank, 8 by 5 by 2 cm.
13. Large, irregular exostoses over the left hip joint and greater trochanter.
14. Bilateral knock knee deformities with large irregular exostoses on the condyles of both femurs and tuberosities of the tibiae and on the right patella.
15. Deformity and irregular exostosis of os calcis and tarsals of the left foot.
16. Hard, firm, opaque mass 1 cm. in diameter in the upper portion of the left epididymis.
17. Scars of previous osteotomy operations over femurs and tibiae.
18. The upper extremities were thin but presented no gross abnormalities or osseous deformities.



Fig. 2A.—Roentgenogram at age of seven years. This lateral view shows two large osteomas of the outer table of the calvarium.

Progression of the deformities is shown in Fig. 1, B and C. The blood Wassermann and Kahn tests were negative. Hemoglobin was 60 to 65 per cent.

Because of the pigmented areas, the multiple soft tissue tumors and the extensive osseous involvement, a tentative diagnosis of von Recklinghausen's neurofibromatosis was made. Examinations of portions of the bony tumors excised at the time of subsequent attempts to correct the deformities by osteotomy failed to show the microscopic picture of neurofibromas.

Oct. 9, 1929.—The small exostosis in the superior line of the left orbit was excised. This was covered with fibrous tissue and was spongy within. A pea-sized pigmented tumor was also removed from the left lower lip. The orbital mass proved to be a dense exostosis containing no cartilage. The soft tumor from the lip showed a mass of connective tissue in bundles of striated muscle containing some hair follicles. There was no evidence of neoplastic change or of neurofibroma.

Aug. 29, 1932.—A unilateral epiphyseal arrest was performed on the medial side of the distal femoral and proximal tibial epiphyses. Microscopic sections of the tissue removed showed normal bone and cartilage.

The patient was readmitted at intervals for observation and in January, 1933, he developed a right otitis media which has continued to discharge. The last hospital admission was in May, 1936. At this



Fig. 4.—Anteroposterior roentgenogram of lumbosacral spine and pelvis, Dec. 21, 1935, aged thirteen years. Large bony growths jut from the upper margins of both acetabula. The right caput and collis femoris are deformed and there is marked lifting of the lower margin of the right acetabulum.

time all of the deformities had increased so that walking was possible only with the aid of a cane. The skin and the subcutaneous tissue over the sole of the left foot have gradually hypertrophied until it presents the appearance of a coarsely corrugated, brownish mushroom-like growth. He has continued to attend school and to maintain his work with the average of his class.

#### DISCUSSION

Many reports of exostoses or of enchondroses involving one or more bones of the body may be found in the literature, but general skeletal

In examination of the knees (Fig. 5), the patellae were irregular, enlarged, and several bony masses were present anteriorly in the soft tissues below the right knee.

In the feet (Fig. 6), a mass of bone representing paraosteal ossification was present on the posteroinferior surfaces of the left calcaneus, and a smaller growth was present on the inferior aspect of the left cuboid. The cauliflower-like changes of the skin over this os calcis are shown in Fig. 7. A composite diagrammatic presentation of the skeletal changes is shown in Fig. 8.

Operations since his first admission to the University of Chicago Clinics include:

*Sept. 4, 1929.*—A large soft tumor 10 by 6 by 2 cm. was excised from the left flank, and this was found to be a flat oval lipoma. At the same time the tumor in the left epididymis was excised and proved to be a bluish cyst about 1 cm. in diameter. Microscopic examination revealed a hemorrhagic papillary cystoma.



Fig. 3.—Roentgenogram, Dec. 21, 1935, aged thirteen years. Anteroposterior view of the cervical and upper thoracic spine. Bony growths may be noted on the transverse processes of the fifth and sixth cervical vertebrae.

*Sept. 10, 1929.*—A marble-sized mass of irregular bone was removed from the left cuboid on its plantar surface, and osteotomies were performed on the tibiae in an attempt to correct the genu valgum deformity. The mass of bone removed from the foot was studied microscopically and consisted of cancellous bone with some fibrous callous. There was no picture of true tumor bone. The section from the site of the osteotomy in the tibia revealed a thin cortex with thick fibrous periosteum. The cancellous bone was atrophic and the marrow spaces were filled with fat.



Fig. 6.—Lateral roentgenogram of the left foot, aged thirteen years. There is bizarre overgrowth of paraosteal bone about the calcaneus and cuboid bones with fusion at the lateral side of the transverse tarsal joint. A portion of the osseous mass has been removed from the cuboid. The free bony piece previously seen above the calcaneus has enlarged and united to both calcaneus and talus.



Fig. 7.—Dec. 21, 1935, aged thirteen years. The outer aspect of the left foot, showing the cauliflower hypertrophy of the skin; tumor growths from the calcaneus, and the fifth toe, and extreme deformity of the member.



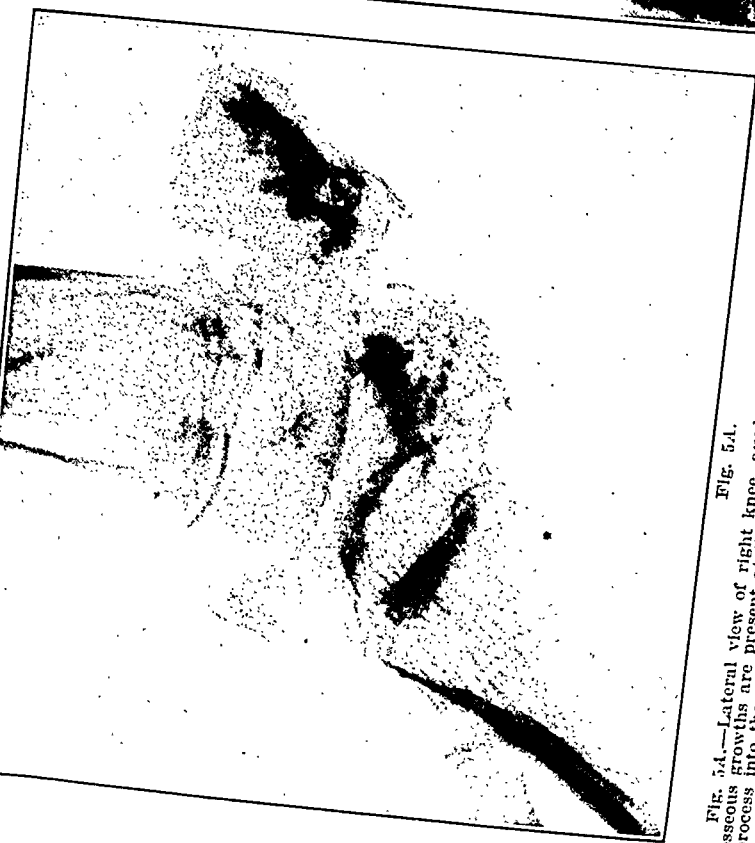


Fig. 5A.—Lateral view of right knee, aged thirteen years. The ossaceous growths are present at the posterior aspect of the joint.

Fig. 5B.—Lateral view of left knee, aged thirteen years. Note the new bone formation in the articular area and the subluxation of the tibia on the femur.



Fig. 5B.

The overgrowth of the patella and its apparent union to the femur is seen. Two free bony processes are present at the posterior aspect of the joint. The upper tibial epiphysis has hypertrophied and extends as a wedge-shaped bony process into the articular area and the subluxation of the tibia on the femur.



Fig. 6.—Lateral roentgenogram of the left foot, aged thirteen years. There is bizarre overgrowth of paraosteal bone about the calcaneus and cuboid bones with fusion at the lateral side of the transverse tarsal joint. A portion of the osseous mass has been removed from the cuboid. The free bony piece previously seen above the calcaneus has enlarged and united to both calcaneus and talus.



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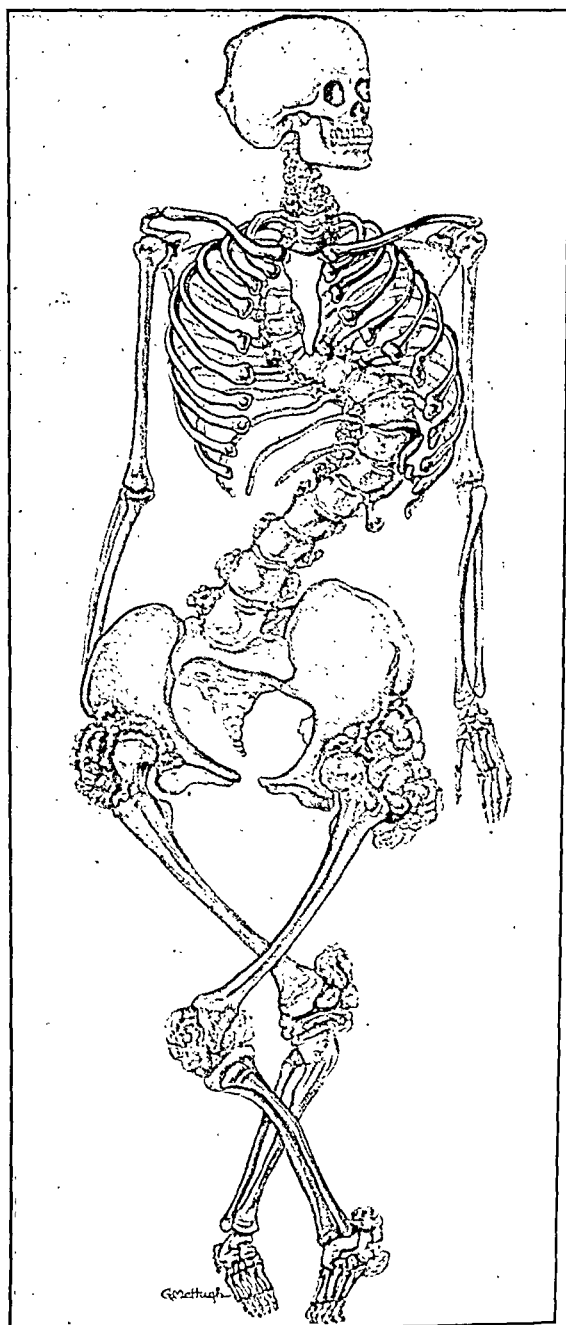


FIG. 8.—Diagrammatic composite drawing of the skeleton showing the extensive deformities and multiple masses of epiphyseal and paraosteal new bone.

deformity is rarely caused by or associated with these typically benign growths. Kaufmann<sup>4</sup> describes a case designated as *exostosis cartilaginea multiplex*, in which numerous chondral tumors existed at different sites on the skeleton. Particularly in this type of case may the pelvis be involved and deformed, producing an *acanthopelvis* or a *pelvis spinosa*. Multiple bony exostoses may occur in the region of the acetabulum and pelvic joints, and these often encroach upon the pelvic cavity. In our case however, the typical cartilage cap on the cartilaginous exostoses was lacking, and although some microscopic sections show cartilage-like cells such as may be found in callus, the growths are definitely osseous.

Edberg,<sup>1</sup> in a study of seven cases of multiple exostoses of the long bones, attributes the condition to regressive or aplastic changes in the thyroid. Von Haberer<sup>2</sup> noted that these multiple tumors frequently lead to growth disturbances of the bones because of encroachment on the epiphyseal lines. Kaufmann also describes the coincident occurrence of pigmented spots, telangiectatic formations, and lipomas. He believes that the multiple cartilaginous exostoses originate from cartilage islands displaced from the growth cartilages. In one of his cases, the subject showed over a thousand exostoses, but there was no general skeletal deformity. Exostoses of the calvarium tend to be static, exist at the time of or shortly after birth, and do not show comparable tendency to enlargement shown by similar tumors on the long bones.

In the case which we are reporting, progression of the deformities in spite of vitamin D medication would seem to eliminate rickets as an etiologic factor. Von Recklinghausen's disease of bone was excluded by finding normal mineral metabolism and by microscopic study of the bones themselves. Generalized neurofibromatosis with skeletal involvement was considered but microscopic sections of neither the bone nor the soft tumors showed the picture characteristic of this disease. Normal renal function excludes renal rickets. The etiology of the disease may be one of primary germ cell injury or defect and therefore a congenital developmental anomaly.

#### SUMMARY

1. A case of progressive osteodystrophy of unexplained etiology with marked skeletal deformities and multiple benign tumors of bones, skin, and subcutaneous tissue has been described.
2. The skeletal features of this case include the formation of massive, irregular exostoses of the calvarium, mandible, thorax, spine, pelvis, femora, tibiae, and left os calcis, associated with deformities of both lower extremities, marked scoliosis, and normal upper extremities.
3. Medical and surgical treatment failed to check the progress of the disease.

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## SPINA BIFIDA OCCULTA

### WITH REPORT OF A CASE IN WHICH THERE WAS AN OCCULT MYELOMENINGOCELE

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SPINA bifida occulta is not an uncommon finding in routine roentgenograms of the spinal column. In a review of 12,000 such roentgenograms, Sutherland found evidence of spina bifida occulta in more than 5 per cent. In 70 per cent of the cases the first and second sacral vertebrae were the site of involvement; in another 25 per cent, the last lumbar vertebra was involved. In such roentgenograms one or more of the vertebral arches will be seen to be defective in that the two laminae have failed to fuse in the midline. This results in the formation of a defect or hiatus in the bony posterior wall of the vertebral canal. In most instances there is no accompanying visible aberration in the overlying cutaneous and fibromuscular tissues and the enclosed nervous elements function normally. Such cases are of interest, so far as the spina bifida occulta is concerned, only as slight anatomic variations. Steindler has questioned whether the condition should be considered pathologic unless it persists beyond the eighth year of life. Less commonly, however, there are seen cases in which the vertebral defect is complicated by evidence of nervous dysfunction and, usually, by gross evidence of malformation in the overlying tissues. These patients present interesting problems in diagnosis and treatment. They come to the attention of pediatricians, urologists, orthopedists, neurologists, and neurosurgeons.

#### ANATOMIC AND PATHOLOGIC CONSIDERATION

Spina bifida occulta has been well defined by Bucy as "a condition in which there is a defect in the posterior neural arches without any externally visible malformation of the spinal cord, its nerves or meninges." When such a malformation is visible externally, it is termed spina bifida cystica (or more commonly, simply spina bifida) and may be further subdivided into meningocele, meningomyelocele, and myelocele.

The origin of these related defects may best be understood by tracing briefly the normal development of the involved structures.<sup>20</sup> The neural tube, from which will evolve the spinal cord and its nerves,

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and the skin of the back are both derivatives of a single sheet of epiblastic (ectodermal) tissue. The neural tube has formed and is completely separated from the overlying skin by the end of the third week of fetal life. At the same time layers of mesoblastic (mesodermal) tissue have interposed themselves between the skin and neural tube and have joined in the midline. From these are derived the spinal meninges, the vertebral column, and the overlying muscles and fibrous tissue. The vertebral bodies have formed and their arches are closed by the end of the eleventh week of fetal life. At the time of their formation, the spinal cord and the vertebral column are of equal length and each segment of the spinal cord lies opposite the corresponding vertebral body. The paired spinal nerves pursue a direct course from the spinal cord to the intervertebral foramina. From the third month of fetal life on, however, the growth of the spinal cord fails to keep pace with that of the spinal column. As a result, the lower end of the spinal cord, the *conus medullaris*, comes to lie progressively higher and higher in the vertebral canal, until in the adult it reaches only to the lower border of the first lumbar vertebra. During this (apparent) ascent of the spinal cord, its nerves have necessarily become elongated and now pursue a diagonal course to the intervertebral foramina. This elongation is the most marked in the lumbosacral region and results in the formation of the aptly named *cauda equina*. The spinal cord retains a permanent connection with its original site of termination by means of the *filum terminale*, a thin fibrous strand extending from the tip of the *conus medullaris* to the posterior surface of the coccyx.

*Spina bifida* in any of its forms represents a perversion or arrest of this normal scheme of development of the spinal cord and its coverings. Specifically, it is a failure of the neural tube to close properly in the midline or to separate completely from the overlying skin. Furthermore, the mesodermal tissues either fail to fuse or are prevented from fusing in the midline. The etiologic factors underlying these perversions of development are apparently many and complex, and may vary in different cases.<sup>22</sup> Some authors have postulated that the primary defect lies in the neural tube itself (Fuchs). Recently, the importance of the mesodermal structures has been emphasized by Dittrich, who pointed out that the bony tissue is phylogenetically the youngest, and, therefore, presumably the least stable tissue present. Whatever the noxious influences may be, they must be active during the early weeks of fetal life.

The anatomic findings in cases of *spina bifida occulta* are extremely variable. By definition, the only constant feature is a defective formation or closure of one or more vertebral arches. One or more vertebrae may be involved, most commonly the last lumbar or first sacral.

The cervical vertebrae are less frequently involved and the thoracic vertebrae are only rarely involved. The vertebral laminae are absent, foreshortened, or malformed and do not meet in the midline. They may be of normal length but may lie in different planes and therefore may not meet.<sup>14</sup> There is no spinous process. It must be noted, however, that defects apparent in roentgenograms taken during childhood may be more apparent than real in that they may represent normally formed but, as yet, imperfectly calcified laminae.

In some cases, including most of those in which there are clinical symptoms, the presence of spina bifida occulta will be betrayed by the appearance of the overlying skin. There may be a small depression or dimple over the vertebral defect. In the lumbosacral region this is known as the fovea coccygea or fovea sacralis; it has been regarded as a certain indication (in the adult) of an underlying spina bifida occulta.<sup>7</sup> In some cases a thick patch of hair, an area of pigmentation, or an area of telangiectasis may overlie the defect. In still other cases, a fibrolipomatous mass will occupy the subcutaneous tissues and cause a gentle elevation of the surface of the skin.

The hiatus in the defective vertebral arch may be patent or it may be closed by a tough membrane, which von Recklinghausen named the "membrana reuniens posterior." This may, in some instances, become much thicker than the bone which it replaces and may then protrude into the vertebral canal, narrow its diameter, and at times compress the spinal cord. The membrane frequently is attached to the overlying skin by a tough band of connective tissue. It may, likewise, be attached to the underlying dura. At other times there may be a cleft in the membrane through which passes a fibrous strand that connects the skin and dura. This strand may, at times, be canalized and form a so-called congenital dermal sinus which is comparable to a pilonidal cyst (Walker and Bucy). Any of these unnatural attachments to the dura may angulate it, produce deformity of the dural sac and at times cause compression of the enclosed cord and nerves.

The defects in the nervous tissues are of greatest importance but little is known about them. Frazier and Dittrich expressed the opinion that in cases of spina bifida occulta the spinal cord and its nerves are usually normally developed and that any degeneration in them is secondary to pressure from deformed meninges and vertebrae. Mixer observed that the nerve tissue, as seen at operation, is usually deformed; the most common malformation is a fusion of the cauda equina into a single irregular bundle which has the appearance of a small spinal cord. Fuchs maintained that the spinal cord is always deformed in cases of spina bifida occulta and applied the term "myelodysplasia" to this condition. He reported several cases in which the failure of dorsal fusion was limited to the spinal cord; the verte-



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brae were normal. Woltman also has reported three such cases. Much of the confusion evidenced by these discordant opinions may be attributed to differences in the definition of terms and to a surprising paucity of careful anatomic studies of cases of spina bifida occulta. In the absence of such knowledge, positive statements are not warranted. It is certain, however, that what may grossly appear to be a normal spinal cord will be found, upon careful examination, to be hydro-myelic; that is, to have an abnormally large central canal, presumably the result of faulty closure of the neural tube. Such a defect need not impair the function of the cord unless it be present in marked degree. At times the spinal cord is found to terminate at an abnormally low level.

Some of the defects which may be present in the spinal dura have already been mentioned. The dura may be enlarged generally or locally. In the latter case the outpouching of dura will constitute a meningocele; or if it contains nerve elements, a myelomeningocele, which in this case will be occult since, by definition, it cannot make its presence known by visible protrusion. Such an occult meningocele or myelomeningocele will usually pass through the hiatus into the subcutaneous tissue, but not to the surface of the skin. We have encountered a case (to be related in detail later in this paper) in which a hitherto unreported anomaly was discovered; namely, an occult myelomeningocele in which the dural cyst, instead of passing out through the hiatus, remained within the confines of the vertebral canal, where it acted as an extradural tumor of the spinal cord and compressed the fibers of the cauda equina.

The frequent association of benign neoplasms and spina bifida occulta has been noted. Lipomatous masses very commonly are found either in the subcutaneous tissues or in the vertebral canal, where they may lie extradurally or intradurally, intimately attached to the fibers of the cauda equina. They may be of "dumbbell" or "hourglass" shape, with the narrow portion occupying the hiatus in the vertebral arch. Dermoids, when present, usually lie extradurally. Exostoses have been found encroaching on the vertebral canal in the region of a spina bifida occulta.<sup>2</sup> All of these may act as tumors of the spinal cord.

Developmental anomalies elsewhere in the body are frequently noted in conjunction with spina bifida occulta. These may be divided into those which are coincidental, as hydrocephalus, absent vertebrae, cleft palate, congenital dislocation of the hips, syndactylism, cryptorchidism and ectopia of the bladder; and those which may be presumed to be secondary to the neurologic defect inherent in the spina bifida occulta, as pronated feet, talipes equinus, and hammer toes.

## SYMPTOMS

The symptoms of spina bifida occulta, when any are present, are the result of neural dysfunction. Unless present from birth or infancy, they commonly make their appearance at the time of puberty or during early adult life. This circumstance is related to the fact that there occurs at this time a period of rapid body growth, as a result of which mechanical stresses are applied to the nervous tissues. The malformed spinal cord and meninges may be prevented by unnatural attachments from undergoing the changes incident to the lengthening of the cauda equina. Abnormal structures, such as the membrana reuniens and benign tumors, may enlarge to a point where they begin to compress the nervous elements. It has likewise been proposed that the myelodysplastic spinal cord may be less able to withstand normal stresses than the normal spinal cord.

The symptoms produced by spina bifida occulta will, of course, vary with the segment of the spinal column involved. Practically, however, lumbosacral spina bifida occulta is most worthy of consideration since it occurs so much more frequently than any other form. The most common symptoms of lumbosacral spina bifida occulta are related to the urinary tract; persistent enuresis is an outstanding symptom. Among twenty-two adults who had nocturnal enuresis, Peritz found that 68 per cent had lumbosacral spina bifida occulta; among a like number of children, the incidence of spina bifida occulta was 35 per cent. More serious interference with the neuromuscular function of the urinary tract may produce urinary retention, with or without overflow incontinence, and may lead at times to hydro-ureter and hydronephrosis. Mertz attributed the "idiopathic congenitally dilated ureter" to spina bifida occulta. Impotence may occur among men. Rectal dysfunction is much less frequent than vesical dysfunction.

Motor and sensory disturbances may occur in any segment of the spinal column. Lumbosacral lesions may produce the syndrome of tumors of the conus medullaris or cauda equina. The paralysis in the extremities may be flaccid or spastic; foot-drop is a common symptom. If the paralysis is present for a considerable time, muscular atrophy will supervene. So-called virginal prolapse of the uterus, appearing in infancy or among nulliparous women, has been attributed to weakening of the muscles of the pelvic floor secondary to spina bifida occulta.<sup>8</sup> Interference with the motor and vasomotor nerves to the lower extremities by spina bifida occulta has been considered a frequent cause of hollow and clawed feet and hammer toes, particularly when these deformities make their appearance or become progressively worse after birth.<sup>1, 21</sup>

The most frequent type of sensory disturbance associated with lumbosacral spina bifida occulta is one limited to the sacral and lower

lumbar segments, a so-called saddle anesthesia. Other distributions may, of course, occur. Thermal anesthesia, which is said to be more marked than other qualities of sensation, may lead to serious burns. Pain of sciatic distribution rarely is a symptom.

Another group of symptoms closely related to the motor and sensory paralyses are the so-called trophic disturbances. These are common about the feet in cases of lumbosacral spina bifida occulta; they have been observed in the hands in cases of cervical spina bifida occulta. Ulcers are prone to form and reluctant to heal. An indolent ulcer should always make one suspicious of spina bifida occulta. The skin may be thin and glazed, and terminal atrophy and gangrene of the digits have been seen.

The weakening of the skeletal structure of the back as a result of spina bifida occulta has been considered a cause of low back pain and habitual scoliosis. The etiologic relationship here is speculative.

#### DIAGNOSIS

The diagnosis of spina bifida occulta is easily made if the condition is suspected. Physical examination may suggest the diagnosis even when the condition is not suspected. One of the lesions of the skin may direct attention to the spinal column. The examining finger may detect the absence of one or more vertebral spines and pressure over this defect may cause pain which will extend to the extremities.<sup>4</sup> Roentgenograms of the spinal column furnish objective evidence of the vertebral defect and its extent. In the presence of such a defect and in cases in which the characteristic symptoms are present, careful neurologic examination should be made and the functional state of the vesical sphincters should be determined. Other possible causes of the symptoms must, of course, be eliminated before attributing them to spina bifida occulta.

The most important step in the diagnosis is an estimation of the relative rôles played by myelodysplasia and by mechanical compression of nerves in the production of the symptoms. Such an estimate is essential, for on it depends to a large degree the adoption or rejection of surgical treatment. Careful consideration of the history, with particular reference to the chronology and progression of the symptoms, and careful consideration of the present neurologic status of the patient are necessary. Defects and dysfunctions which were present at birth and have not been progressive are likely to be the result of malformation or permanent injury of the spinal cord and nerves. When the symptoms make their appearance during life, particularly if they are progressive, mechanical interference with nerve function is suggested. Both congenital and mechanical lesions may, of course,

be present together in any case. The introduction of radiopaque oil (lipiodol) into the subarachnoid space, with subsequent roentgenoscopic and roentgenographic observation of its movement and distribution, occasionally has been found valuable in visualizing the condition of the nerves and the presence of subarachnoid block.<sup>14, 17</sup> However, this procedure is not entirely without risk and should rarely be necessary. Lumbar punctures should be performed with great care in the region of a spina bifida occulta, as there is danger of injuring abnormal nerve tissue.<sup>1</sup>

We have observed a case which illustrates well a number of points in connection with the diagnosis and treatment of spina bifida occulta and which demonstrated the beneficial results of neurosurgical intervention in suitable cases. There also was a unique pathologic finding.

#### REPORT OF CASE

A man, aged thirty-eight years, registered at the Mayo Clinic on Aug. 15, 1935, complaining of deformity and chronic infection of his left foot which had been present for ten years. He was the father of a normal child. Ten years before he came to the clinic a "hammer toe" deformity of the second toe of the left foot had developed; this had been corrected surgically. Shortly thereafter, the patient had run a nail into the sole of his left foot near the head of the second metatarsal bone. An ulcer had developed at this point and had drained intermittently. Flexion deformities of several other toes also had developed later and the patient had noted the appearance and gradual spread of anesthesia over his left foot. In recent months, before he came to the clinic, he had been forced to use crutches in order to get about, because painful and infected callosities had developed on the sole and heel of the left foot.

Examination revealed a small dimple in the skin over the lumbosacral junction. There was a hammer-toe deformity of the second toe of the right foot. The second toe of the left foot had been surgically removed. The skin of the left foot was smooth and thin; on the plantar surface, between the heads of the second and third metatarsal bones, was a draining sinus. The lateral aspect of the heel was covered with a chronically infected callosity. Neurologic examination revealed that the muscles of the right leg and right foot were moderately weak and slightly atrophied. The hamstring reflex and Achilles reflex were absent on the left side. There was a definite hyperesthesia to all forms of sensation over the left foot and lateral aspect of the left leg. Laboratory examination of the blood and urine did not reveal anything abnormal. A flocculation test for syphilis was negative. Roentgenograms of the left foot showed no active infection in the metatarsal bones. The roentgenogram of the lumbosacral region revealed a spina bifida occulta of the first sacral segment with deformity of the arch of the last lumbar vertebra. A diagnosis of spina bifida occulta with myelodysplasia was made and exploration was advised.

On Aug. 23, 1935, one of us (J. G. L.) performed laminectomy through a mid-line skin incision with the sacral dimple as its midpoint. When the deformed laminae of the last lumbar and first sacral vertebrae were removed, there was exposed a bulging tumor which had the appearance of the dural sac and which pulsed as does the normal spinal dura (Fig. 1a). The laminae of the fourth lumbar vertebra were removed; they were found to be thinner than normal. The tumor could

lumbar segments, a' so-called saddle anesthesia. Other distributions may, of course, occur. Thermal anesthesia, which is said to be more marked than other qualities of sensation, may lead to serious burns. Pain of sciatic distribution rarely is a symptom.

Another group of symptoms closely related to the motor and sensory paralyses are the so-called trophic disturbances. These are common about the feet in cases of *lumbosacral spina bifida occulta*; they have been observed in the hands in cases of *cervical spina bifida occulta*. Ulcers are prone to form and reluctant to heal. An indolent ulcer should always make one suspicious of *spina bifida occulta*. The skin may be thin and glazed, and terminal atrophy and gangrene of the digits have been seen.

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The most important step in the diagnosis is an estimation of the relative rôles played by myelodysplasia and by mechanical compression of nerves in the production of the symptoms. Such an estimate is essential, for on it depends to a large degree the adoption or rejection of surgical treatment. Careful consideration of the history, with particular reference to the chronology and progression of the symptoms, and careful consideration of the present neurologic status of the patient are necessary. Defects and dysfunctions which were present at birth and have not been progressive are likely to be the result of malformation or permanent injury of the spinal cord and nerves. When the symptoms make their appearance during life, particularly if they are progressive, mechanical interference with nerve function is suggested. Both congenital and mechanical lesions may, of course,

On the other hand, severe paralysis of the lower extremities, which has been present since birth, is regarded as a contraindication to operation.

Brickner suggested that operation be undertaken in all infants and children in whom spina bifida occulta was associated with subcutaneous lipomas or areas of hypertrichosis, whether symptoms were present or not, the aim being to forestall future trouble. Most authors regard this as too radical an attitude. It is also agreed that enuresis of childhood, without other symptoms, is not an indication for operation, and even when it occurs among adults Bucy warns against laminectomy when the condition is mild, because even slight operative trauma to the nerves may make the condition worse than it already was. This injunction may well be borne in mind in all cases of this type.

Operation should be considered, however, in all cases of severe urinary dysfunction, especially if the symptoms appear or become worse at the time of puberty (Mixer). Mertz reviewed seventy-nine reported cases in which laminectomy was performed for spina bifida occulta which was associated with disturbance of the nervous control of the lower part of the urinary tract. In half of these cases the patients were relieved and in the other half of the cases the patients were helped, although relapses were common. He noted, as have others, that operation may benefit certain of the patients' symptoms and not others. Patients who have trophic lesions, such as perforating ulcers, are often favorable subjects for operation.<sup>12</sup>

It is likewise agreed that operation for relief of deformities of the pedal extremity, such as talipes equinus, should be undertaken only in the face of a progressive lesion. Hackenbroch operated in seventy such cases; beneficial results were obtained in half of the cases in which definite abnormalities were found in the epidural space.

Since it is impossible to predict with certainty what will be found at the time of operation, disappointing results will often follow laminectomy in cases of spina bifida occulta. However, in consideration of the very low operative mortality and the very definite benefits which frequently accrue, operation should be seriously considered in every case.

The operative procedure employed will vary in each case. In any event, a laminectomy is performed in the region of the defect, and sufficient bone is removed to permit a thorough inspection of the dural sac. In most instances it will be wise to open the dura for inspection of the cauda equina, if only to be able to estimate the prognosis for improvement following the surgical procedure. The measures necessary to relieve mechanical stress on the nervous tissues will, of course, vary with the exact condition found at exploration, and must be decided on at the time of operation. Great care must be exercised not to injure already incompetent nerves.



then be seen to arise from the dorsal surface of the normal dura at a point opposite the laminae of the fourth lumbar vertebra and to extend caudally to the level of the defect in the arch of the first sacral vertebra, but to remain confined entirely within the limits of the vertebral canal. The tumor was cystic. When opened it was found to contain cerebrospinal fluid and to communicate with the spinal subarachnoid space by means of a small ostium through which projected a mass of tissue which appeared to be continuous with the spinal cord; that is, to represent an aberrant mass of nerve tissue (Fig. 1b), possibly an elongated conus medullaris. This was dissected free from the sac and replaced within the spinal subarachnoid space. The myelomeningocele sac was then severed from the dura (Fig. 1c) and a plastic closure of dura and subcutaneous tissues was made. The lumbosacral fascia was sewed together in the midline.

Postoperative convalescence was uneventful. Within two weeks after the operation, the patient said that the foot felt better. Neurologic examination did not show any change from the preoperative condition except that the ulcer on the sole of the left foot had healed. The patient was permitted to return to his home at the end

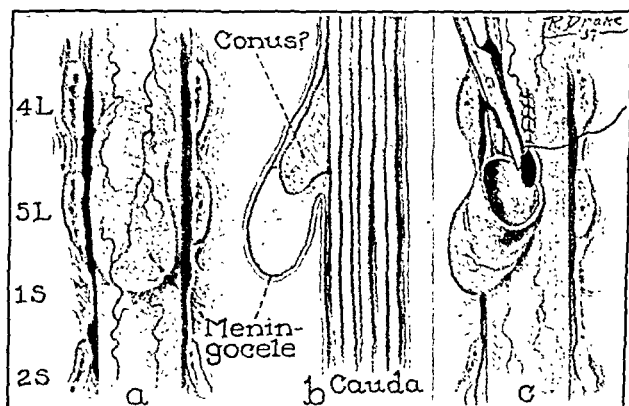


Fig. 1.—a, Failure of development of the laminae of the first sacral vertebra and thinning of the laminae of the fourth and fifth lumbar vertebrae from pressure of the occult myelomeningocele; b, diagrammatic lateral view of the tumor and cauda equina; c, resection of the meningocele and plastic closure of the dura mater.

of the third week. He has since reported that the ulcer has remained healed and that the callosities of his heel are less troublesome. He is able to get about without aid and with comfort.

#### NEUROSURGICAL TREATMENT

The neurosurgical treatment of spina bifida occulta is directed toward improving nerve function by relieving mechanical interference. Obviously, nothing can be done to improve the function of malformed or degenerated nerve tissue. We already have considered the diagnostic aspects of this problem.

It is impossible to set forth hard-and-fast rules to govern the adoption or rejection of operative treatment. So many factors enter into each case that one can only indicate general principles. It is generally agreed that only severe and progressive symptoms call for exploration.

On the other hand, severe paralysis of the lower extremities, which has been present since birth, is regarded as a contraindication to operation.

Brickner suggested that operation be undertaken in all infants and children in whom spina bifida occulta was associated with subcutaneous lipomas or areas of hypertrichosis, whether symptoms were present or not, the aim being to forestall future trouble. Most authors regard this as too radical an attitude. It is also agreed that enuresis of childhood, without other symptoms, is not an indication for operation, and even when it occurs among adults Bucy warns against laminectomy when the condition is mild, because even slight operative trauma to the nerves may make the condition worse than it already was. This injunction may well be borne in mind in all cases of this type.

Operation should be considered, however, in all cases of severe urinary dysfunction, especially if the symptoms appear or become worse at the time of puberty (Mixer). Mertz reviewed seventy-nine reported cases in which laminectomy was performed for spina bifida occulta which was associated with disturbance of the nervous control of the lower part of the urinary tract. In half of these cases the patients were relieved and in the other half of the cases the patients were helped, although relapses were common. He noted, as have others, that operation may benefit certain of the patients' symptoms and not others. Patients who have trophic lesions, such as perforating ulcers, are often favorable subjects for operation.<sup>12</sup>

It is likewise agreed that operation for relief of deformities of the pedal extremity, such as talipes equinus, should be undertaken only in the face of a progressive lesion. Hackenbroch operated in seventy such cases; beneficial results were obtained in half of the cases in which definite abnormalities were found in the epidural space.

Since it is impossible to predict with certainty what will be found at the time of operation, disappointing results will often follow laminectomy in cases of spina bifida occulta. However, in consideration of the very low operative mortality and the very definite benefits which frequently accrue, operation should be seriously considered in every case.

The operative procedure employed will vary in each case. In any event, a laminectomy is performed in the region of the defect, and sufficient bone is removed to permit a thorough inspection of the dural sac. In most instances it will be wise to open the dura for inspection of the cauda equina, if only to be able to estimate the prognosis for improvement following the surgical procedure. The measures necessary to relieve mechanical stress on the nervous tissues will, of course, vary with the exact condition found at exploration, and must be decided on at the time of operation. Great care must be exercised not to injure already incompetent nerves.

## SUMMARY

Spina bifida occulta is a developmental defect of the spinal cord, its meninges, the vertebral column, and the overlying muscular and cutaneous tissues. It begins in early embryonic life. A review of the literature emphasizes the wide variety of anatomic malformations which may occur. These may be divided into those which affect the nervous tissues themselves (myelodysplasia) and those which occur in the mesodermal tissues surrounding and supporting the spinal cord, including its meninges. In most instances these defects will not be great enough to compromise the function of the spinal cord and its nerves. The condition will remain subclinical but may be recognized in roentgenograms of the spinal column.

When clinical symptoms accompany spina bifida occulta, they usually are the result of neural dysfunction. This may result from defects inherent in the nervous tissue (myelodysplasia) or from mechanical interference with the function of nervous tissue by the tension or pressure of adjacent tissues. The most common symptoms are those which are related to the urinary apparatus. Motor, sensory, and trophic disorders about the lower extremities are likewise common and should always arouse the suspicion of spina bifida occulta. Pain is rarely a symptom. Certain malformations of the feet and toes (talipes equinus, hammer toes) have been attributed to spina bifida occulta in many cases. Once spina bifida occulta is suspected, it is easily verified.

Surgical treatment, in the form of exploratory laminectomy and attempted relief of mechanical interference with nerve function, should be considered in every case in which the symptoms appear or become progressively worse during postnatal life. Although only partial relief of symptoms may be expected in most cases, the low mortality of the surgical procedure justifies its trial in most instances.

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joint. Rebaudi<sup>15</sup> (1934) reported 14 cases, and Buzby<sup>16</sup> (1936) recorded 13 elbows successfully resected out of 15 in a series of 14 cases, 3 of these for tuberculous arthritis. Most recently, Magnusson<sup>17</sup> (1936) has reported the combined resection and interposition of fascia lata in 17 cases of tuberculosis of the elbow, with satisfactory motion in 16 and with ankylosis in 1.

#### INDICATIONS

There has been some controversy as to the relative merits of resection of the elbow joint and arthroplastic reconstruction.

We take issue, on the basis of the experience of many others as well as our own, with the statement of MacAusland<sup>18</sup> (1922) that: "The results from this (excision) are very unsatisfactory, the joint being flail, weak and usually requiring external treatment in the form of a leather with limited elbow joint motion. . . . The ultimate results from its use do not warrant its being considered for any condition except tuberculosis of the elbow"; and with that of Campbell<sup>19</sup> (1929): "An arthroplasty is often the only procedure that offers hope for the reestablishment of motion and of function in an elbow severely injured by fractures about the elbow joint." Certainly a more conservative note is struck by Jones and Lovett:<sup>20</sup> "It is an open question whether this operation (arthroplasty) has sufficient advantage over excision to warrant one in pronouncing it the operation of election."

Arthroplasty, introduced as a refinement of excision, has for its chief object not only the interposition of a layer of fascia or membrane, but the reconstruction of the bone ends, in such a way as to adopt the opposing surfaces and so give stability as well as movement to the new joint. In an attempt to avoid the slight instability that often follows a resection and the occasional flail elbow, French surgeons resorted to a less free removal of bony tissue and attempted to avoid reankylosis by interposing muscle tissue. Many interposing media have been utilized—inorganic substances, fat, pedicled fascia fat (Murphy),<sup>21</sup> animal membrane (Baer),<sup>22</sup> heterogenous fascia, and autogenous fascial transplants (Putti,<sup>23</sup> Hey-Groves,<sup>24</sup> MacAusland,<sup>25</sup> Campbell,<sup>26</sup> Albee,<sup>27</sup> and others).

However, a moderate degree of lateral instability in a resected elbow does not represent a disability as the elbow is a nonweight-bearing joint, while a flail elbow is an infrequent occurrence, following only very extensive resections. Large series of resected cases have demonstrated the restoration of very satisfactory function. The attempt in arthroplasty to restore the anatomic conformation of the joint and to prevent instability by a minimum amount of bony sacrifice and the interposition of fascia harbors the greater possibility of reankylosis, as has been shown experimentally by Allison and Brooks and as has been proved clinically in many instances.



## RESECTION OF THE ELBOW JOINT

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### REVIEW OF LITERATURE

ALTHOUGH Hippocrates and Celsus both alluded to the removal of the articulating extremities of dislocated bones, the first application of resection to the elbow joint is attributed to Wainmann<sup>1</sup> in 1758. Macartney<sup>2</sup> noted that the procedure was practiced in the last decades of the eighteenth century by Filkin (1786), Moreau (1794), and Park (1794). Cases, successfully resected, were reported by Nickels<sup>3</sup> in 1837 and two years later by Bier.<sup>4</sup> The procedure gained its place in British surgery only after the enthusiastic recommendation of Syme,<sup>5</sup> and was first performed in America independently by Buck<sup>6</sup> and Pancoast<sup>7</sup> in 1842.

A variety of techniques have been described by Langenbeck, Kocher, Park, Moreau, Heuter, Chassaignac, Dupuytren, Faraheuf, and Nélaton.<sup>8</sup> Its greatest proponent was Ollier,<sup>9</sup> who wrote profusely on his method, and who performed a total of 270 resections from 1859 to 1900. In the Musée Ollier are 120 elbow joint specimens, 86 of these resected for tuberculosis.

The early literature abounds with numerous articles and monographs on the resection of joints, but in recent years this has been greatly supplanted by the interest of surgeons in arthroplasty. Between the years 1837 and 1883, 235 authors contributed numerous reports, and 39 monographs were printed, on resection of the elbow joint, with noteworthy contributions by Hodges<sup>10</sup> in 1861 of 119 cases and by Culbertson<sup>11</sup> in 1876 in his prize essay including 1,082 elbow joint resections collected from the world literature, and from 1883 to 1900 over 180 authors added many more articles and monographs. Between 1900 and 1925, 75 articles and 6 monographs were published, and since then only 13 authors have contributed on this subject.

Comte<sup>12</sup> in 1925 studied 55 of Ollier's resections for tuberculous arthritis of the elbow joint, followed from five to sixty years, with 94 per cent satisfactory results, and 100 per cent excellent results in 21 resections for nonspecific arthritis and malunited, disabling fractures. Sorrel, in commenting on Gruea's<sup>13</sup> four cases (1932), stated that he had performed 50 resections with a high percentage of success. Nové-Jossierand and Pouzet<sup>14</sup> (1932) have utilized resection and hemiresection in the treatment of chronic, irreducible dislocations of the elbow

reankylosis. The osteoplastic activity of the elbow region in young patients is a distressing feature known to all those interested in traumatotherapy. Besides, in young children one cannot resect so freely, as they do not possess a sufficiently well-developed musculature to assure satisfactory stability in a freely resected joint. Finally, the postoperative cooperation, which is so essential to obtain a good result and which is often painful and trying, is found wanting in a child.

#### MODUS OPERANDI

A variety of incisions have been advocated, many so placed as to disregard and indiscriminantly sever the ulnar nerve.<sup>8</sup>

Ollier's method of "resection sous capsulo-périostée," for which he gave credit to Verneuil, aimed at the removal of the bones alone, leaving the periosteum to admit a reformation of all the structures of the joint. Other surgeons have recommended the free sacrifice of all adjacent periosteum and soft tissues in the so-called open method. Ollier's excellent results in great part depended on what he considered as the *sine qua non* of a successful elbow resection, i.e., a liberal excision of bone and the early mobilization of the new joint.

The operation is performed without the use of a tourniquet. It is wise, in an elbow that has not functioned for a long time, to reactivate the muscles preparatory to resection with massage and electrical stimulation.

1. A posterior longitudinal incision is made, extending 3 inches above and 3 inches below the olecranon process.

2. The medial skin flap is retracted and the ulnar nerve is isolated between the medial condyle and olecranon process, freed upwards and downwards, and retracted gently.

3. The triceps tendon insertion and a small portion of the attached olecranon process, severed with an osteotome, are retracted upwards, exposing the posterior portion of the elbow joint. This procedure, employed since 1931, has obviated the residual triceps weakness that followed our previous technique. Several German surgeons, Trendelenburg, Mosetig-Moorhoff, and Spuhn, and Senn, of America, have recommended the preservation of the olecranon process with its attached triceps tendon, reuniting it with metallic pins.

4. The periosteum is elevated laterally and medially from the lower end of the humerus and the upper ends of the radius and ulna, with the attached flexor and extensor muscle groups. This is continued anteriorly until the joint has been completely exposed and the vital structures of the antieubital fossa displaced anteriorly and well protected.

5. The humerus is sawed completely through above the condyles, about 1 inch above the joint surface.

Tuberculosis of the elbow joint occurred in 2 per cent of 224 joints operated upon in Cleveland's<sup>29</sup> series (1935). Resection of this joint is considered by most authorities<sup>20, 30, 31</sup> the operation of election for adult tuberculous arthritis, in the presence of progression despite conservative treatment. Fusion, unlike its application to other joint tuberculosis, has not been so acceptable to the elbow joint, not only because of technical difficulties and the awkwardness of an ankylosed elbow, even in good functional position, but also because it fails to extirpate the disease process and there is a frequency of recurrence and progression. Cleveland<sup>29</sup> writes: "I now believe a careful resection may be a better and more logical procedure in this nonweight-bearing joint. Our record of only one successful fusion in five attempts leaves much to be desired." According to Comte,<sup>12</sup> 55 of Ollier's cases resected for tuberculosis, showed 95 per cent satisfactory results from five to sixty years postoperatively, while Oschman,<sup>30</sup> of Kocher's clinic, reported 70 per cent excellent results in 40 cases (1872 to 1897). Steindler<sup>31</sup> cites Garre's statistics of 51 per cent cures in 235 cases, König's of 54 per cent cures, and Bardenheuer and Lossen's of 63 per cent cures and 70 per cent good functional results. Fatal miliary tuberculosis may ensue, as it may follow the interference of any tuberculous focus, König<sup>32</sup> observing 16 cases, and Wartman<sup>32</sup> 26 cases out of 225 deaths in 837 collected cases of elbow joint resection.

Resection is indicated in ankyloses of all origin, fibrous or osseous, traumatic or infectious in origin. Following pyogenic infections, no interference is advised until several years of quiescence have elapsed and only after a vigorous manipulation fails to activate any latent process. In ankylosis due to rheumatoid arthritis, despite a long quiescent interval with normal clinical and laboratory findings, operative interference may be followed by a reactivation of systemic and local manifestations.

Resection is of value in the rehabilitation of elbow joint fractures with deformity and disability, and in chronic irreducible dislocations. During the World War, considerable was written on the merits of its use following débridement for gunshot wounds and compound fractures of the elbow region. The satisfactory results that not infrequently follow a conservative regime in comminuted simple and compound fractures of the elbow do not warrant such immediate radical therapy in civil surgery.

This operation is valuable in the extirpation of benign and locally malignant osseous tumors.

Although Annandale, Ashhurst, Chassaignac, and others advocated its use in the first decade of life, the experience of most surgeons is that resection is best delayed until the cessation of the growth period, not only to avoid an unsightly shortened extremity, but also to avoid

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Tuberculosis of the elbow joint occurred in 2 per cent of 224 joints operated upon in Cleveland's<sup>29</sup> series (1935). Resection of this joint is considered by most authorities<sup>20, 30, 31</sup> the operation of election for adult tuberculous arthritis, in the presence of progression despite conservative treatment. Fusion, unlike its application to other joint tuberculosis, has not been so acceptable to the elbow joint, not only because of technical difficulties and the awkwardness of an ankylosed elbow, even in good functional position, but also because it fails to extirpate the disease process and there is a frequency of recurrence and progression. Cleveland<sup>29</sup> writes: "I now believe a careful resection may be a better and more logical procedure in this nonweight-bearing joint. Our record of only one successful fusion in five attempts leaves much to be desired." According to Comte,<sup>12</sup> 55 of Ollier's cases resected for tuberculosis, showed 95 per cent satisfactory results from five to sixty years postoperatively, while Oschman,<sup>30</sup> of Kocher's clinic, reported 70 per cent excellent results in 40 cases (1872 to 1897). Steindler<sup>31</sup> cites Garre's statistics of 51 per cent cures in 235 cases, Konig's of 54 per cent cures, and Bardenheuer and Lossen's of 63 per cent cures and 70 per cent good functional results. Fatal miliary tuberculosis may ensue, as it may follow the interference of any tuberculous focus, Konig<sup>32</sup> observing 16 cases, and Wartman<sup>32</sup> 26 cases out of 225 deaths in 837 collected cases of elbow joint resection.

Resection is indicated in ankyloses of all origin, fibrous or osseous, traumatic or infectious in origin. Following pyogenic infections, no interference is advised until several years of quiescence have elapsed and only after a vigorous manipulation fails to activate any latent process. In ankylosis due to rheumatoid arthritis, despite a long quiescent interval with normal clinical and laboratory findings, operative interference may be followed by a reactivation of systemic and local manifestations.

Resection is of value in the rehabilitation of elbow joint fractures with deformity and disability, and in chronic irreducible dislocations. During the World War, considerable was written on the merits of its use following débridement for gunshot wounds and compound fractures of the elbow region. The satisfactory results that not infrequently follow a conservative regime in comminuted simple and compound fractures of the elbow do not warrant such immediate radical therapy in civil surgery.

This operation is valuable in the extirpation of benign and locally malignant osseous tumors.

Although Annandale, Ashhurst, Chassaignac, and others advocated its use in the first decade of life, the experience of most surgeons is that resection is best delayed until the cessation of the growth period, not only to avoid an unsightly shortened extremity, but also to avoid

reankylosis. The osteoplastic activity of the elbow region in young patients is a distressing feature known to all those interested in traumatotherapy. Besides, in young children one cannot resect so freely, as they do not possess a sufficiently well-developed musculature to assure satisfactory stability in a freely resected joint. Finally, the postoperative cooperation, which is so essential to obtain a good result and which is often painful and trying, is found wanting in a child.

#### MODUS OPERANDI

A variety of incisions have been advocated, many so placed as to disregard and indiscriminantly sever the ulnar nerve.<sup>8</sup>

Ollier's method of "resection sous capsulo-périostée," for which he gave credit to Verneuil, aimed at the removal of the bones alone, leaving the periosteum to admit a reformation of all the structures of the joint. Other surgeons have recommended the free sacrifice of all adjacent periosteum and soft tissues in the so-called open method. Ollier's excellent results in great part depended on what he considered as the *sine qua non* of a successful elbow resection, i.e., a liberal excision of bone and the early mobilization of the new joint.

The operation is performed without the use of a tourniquet. It is wise, in an elbow that has not functioned for a long time, to reactivate the muscles preparatory to resection with massage and electrical stimulation.

1. A posterior longitudinal incision is made, extending 3 inches above and 3 inches below the olecranon process.

2. The medial skin flap is retracted and the ulnar nerve is isolated between the medial condyle and olecranon process, freed upwards and downwards, and retracted gently.

3. The triceps tendon insertion and a small portion of the attached olecranon process, severed with an osteotome, are retracted upwards, exposing the posterior portion of the elbow joint. This procedure, employed since 1931, has obviated the residual triceps weakness that followed our previous technique. Several German surgeons, Trendelenburg, Mosetig-Moorhoff, and Spuhn, and Senn, of America, have recommended the preservation of the olecranon process with its attached triceps tendon, reuniting it with metallic pins.

4. The periosteum is elevated laterally and medially from the lower end of the humerus and the upper ends of the radius and ulna, with the attached flexor and extensor muscle groups. This is continued anteriorly until the joint has been completely exposed and the vital structures of the antecubital fossa displaced anteriorly and well protected.

5. The humerus is sawed completely through above the condyles, about 1 inch above the joint surface.

6. The inferior site of resection is now easily exposed by forcing the partially excised elbow posteriorly and well into the wound. If the superior radioulnar joint is intact, it should be preserved and the ulna alone resected just above the radial head. If, however, this joint is involved, the radial head and ulnar upper extremity are excised at a level just above the radial tuberosity. The bared ends are smoothed and rounded off with rongeurs and a bone file. No bone wax is utilized. A total of at least  $1\frac{1}{2}$  to 2 inches must be removed from the humerus, radius, and ulna. It is our experience that the common fallacy is the removal of too little rather than too much bone.

7. A firm stitch of No. 3 chromic catgut is passed through the triceps insertion, and a drill hole, made at the upper end of the ulna, and sutured to the surrounding periosteum, the small olecranon fragment contacting the fresh bony surface of the upper ulna.

8. The deep tissues—periosteum, capsule, muscle, and fascia, are all sutured as one with No. 1 chromic catgut, the subcutaneous tissues with plain catgut, and the skin with dermal or silk sutures. A small rubber drain is inserted at the lower angle of the wound for twenty-four to forty-eight hours.

9. A plaster splint is applied posteriorly with the elbow flexed at a right angle and the entire extremity is suspended to reduce postoperative swelling.

10. Active and passive exercises are instituted as soon as the acute reaction in the operative site has subsided, i.e., as early as the third or fourth postoperative day.

Skin sutures are removed on the tenth day postoperatively and an intensive course of baking, massage, and sinusoidal stimulation to the flexor and extensor muscles of the elbow joint commenced. A sling is worn for three months to prevent abnormal traction on the soft tissues of the elbow region and undue lateral motion. We have found a brace or other external support unnecessary in our cases.

Good active flexion is obtained in two to three months, but complete recovery must not be anticipated in less than six months, until the lax elbow soft structures have adapted themselves to the resection, and concomitantly, lateral instability grows less marked. A residual  $10^{\circ}$  to  $15^{\circ}$  of lateral motion which usually persists is consistent with a satisfactory functional result.

The operation of brachial hemiresection, as practiced in the clinic of Nové-Josserand for chronic, irreducible posterior dislocations of the elbow joint, consists of the removal of a liberal portion ( $1\frac{1}{2}$  inches to 2 inches) of the lower end of the humerus with preservation of the forearm bones. In the antibrachial type of hemiresection, only the upper extremities of the radius and ulna are extirpated.

## REVIEW OF AUTHORS' CASES

The seventeen cases herein presented were operated upon by the senior author (A. J. D.), the first in 1914. Their ages vary from five to forty-six years—3 in the first decade of life, 5 in the second, 2 in the third, 5 in the fourth, and 2 in the fifth. Seven cases were operated upon prior to the cessation of the growth period. There are 2 females and 15 males in the series.

Two of the elbows were the site of proved tuberculosis, one aged five years, the other thirty-six years, with painful and restricted motion. In 13 cases there was complete loss of motion of the elbow joint, with fixation at angles varying from  $90^{\circ}$  to  $165^{\circ}$ , due to comminuted fractures or fracture-dislocations in this region. There were 2 cases of old, irreducible dislocations of the elbow joint.

In 1 case there was a complicating musculospiral nerve paralysis due to involvement of the nerve in callus, and this required liberation of the nerve concomitantly with the resection.

Resection was performed four months to one and one-half years following the onset of disability in 15 cases, and in one case eighteen years and in another thirty-four years following the original injury.

Total resection was performed in 14 cases, the brachial type of hemiresection in 2 cases of old, comminuted fractures of the lower end of the humerus, and the antibrachial type in 1 case of chronic, irreducible fracture-dislocation.

The duration of follow-up study since the performance of the resection in the collected cases varies from six months in 1 case to ten years in 2, with 9 patients observed from one to five years, and 5 from six to nine years.

In 11 of the 17 cases, 9 adults and 2 children aged nine and thirteen years, the results were excellent, with restoration of complete active and passive motion and with lateral motion of only  $10^{\circ}$  to  $15^{\circ}$ . The function in all of these cases is very satisfactory and several have returned to hard manual labor. Five of the cases show some residual extensor weakness against gravity and resistance, while the remaining 6, operated upon since 1931, evidence excellent restoration of this power due to the preservation of the triceps mechanism. In 1 case, some restriction of flexion due to an anterior bony block at the lower end of the resected humerus disappeared in one year following persistent physiotherapy and very gentle manipulation.

In our most recent case, an extensive resection was performed six months ago for tuberculous arthritis with pain and restricted motion, and at present there is a complete restoration of passive motion, with active flexion and extension against moderate resistance. Considerable instability of  $25^{\circ}$  to  $30^{\circ}$  is still present, but this is gradually lessening. The disease process has been extirpated and the prognosis is good.



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4. Its use is contraindicated in children and in young adults prior to the cessation of the growth period, because of the danger of a deficient functional result or of failure.

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In 2 children, aged seven and eleven years, only partial but satisfactory motion has been restored, in the former ranging between 70° and 110°, and in the latter, from complete flexion to 120°. In the former a complicating musculospiral nerve involvement was successfully corrected by neurolysis at the time of resection. A brachial hemiresection had been performed in the other patient for an unreduced fracture-dislocation.

Reankylosis occurred in 3 cases, aged five, eleven, and fifteen years. The first case had tuberculosis of the elbow joint, and developed postoperatively a secondarily infected sinus with a resultant ankylosis at 80°. The other 2 cases had sustained comminuted fractures about the elbow joint. One had a brachial type of hemiresection with reankylosis at 125°. The other, a female, had a total resection but cooperated very poorly in her postoperative regime with resultant ankylosis at 90°.

Postoperative roentgenograms of the successfully resected elbows showed a rounding off and sclerosis of the articulating bony margins, with their approximation until only a narrow joint space intervened. Occasionally bony particles and fragments were noted in the surrounding soft tissues, but these did not vitiate the good function of the nearthrosis. The olecranon fragment, where it had been preserved, became reattached by osseous union. In the 2 children with partial restoration of function and in the 3 with reankylosis, considerable postoperative osteoplastic formation was evident.

In summary, the results of elbow joint resection have been very satisfactory in all of our adult patients (9), but in only 2 children. Of the remaining 5 children, a partial but satisfactory restoration of function has occurred in 2 and ankylosis in 3, 2 of the latter in a good functional position. Brachial hemiresection resulted in a complete ankylosis in 1 child and in a partial ankylosis in another. The anti-brachial type of hemiresection was successfully employed in 1 adult. Total resection was performed in the remaining cases, with 11 successful results, 1 case with partial restoration of motion and 1 case with failure.

#### SUMMARY

1. The procedure of resection of the elbow joint is discussed in detail and the preservation of the triceps mechanism is stressed. Adequate bony excision and early mobilization are its essential features. In our hands total resection has proved far more satisfactory than partial resection.

2. This operation, in adults, is a satisfactory method for the rehabilitation of a partially or completely ankylosed elbow joint.

3. It is, at present, the treatment of choice for tuberculous arthritis of this joint, in adults, where conservative therapy has failed.

4. Its use is contraindicated in children and in young adults prior to the cessation of the growth period, because of the danger of a deficient functional result or of failure.

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## EXTRAFASCIAL APICOLYSIS (SEMB)

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*(From the Department of Surgery, University of Wisconsin Medical School)*

**A**PPROXIMATELY 90 per cent of tuberculous cavities in the lung occur in the upper lobe. Even wide rib resections are occasionally inadequate for closure because the large spherical cavities are converted into longitudinal slitlike spaces which persist in the costo-vertebral gutter anterior to the transverse processes. These failures have been overcome to a certain extent by resecting the transverse processes in the region of the cavity. Some surgeons have attempted to enhance the collapse through plombage and pressure pads, in spite of which certain cavities continue to resist all efforts at closure. The natural tendency, enhanced where possible by artificial pneumothorax, is for a cavity to heal concentrically. This is often prevented because pleural adhesions may fix the lung to the overlying rigid thoracic cage. The effect of thoracoplasty comes about through the application of two mechanical forces; relaxation and collapse. Both result from a reduction in the size of the thoracic cage. This most often occurs laterally because the base and apex are fixed. The efficiency of the collapse depends upon the extent of the removal of the overlying ribs, the condition of the diseased lung, and the fixation of the mediastinum. Frequently the amount of lateral collapse obtained will prove adequate if the cavity is small. Even though the cavity is not entirely collapsed, the closure of the bronchus leading to it will insure against further escape of tubercle bacilli into the tracheobronchial tree. Early thin-walled cavities will usually heal completely, but older cavities with thick avascular and inelastic fibrous walls probably never heal even though collapsed. Success in dealing with these cavities lies in exerting pressure on them from all directions accompanied by closure of the communicating bronchus. During the past ten years we have at times been disappointed with our failure to accomplish this. Even the most radical sacrifice of ribs has failed to render the sputum negative. It was because of our failures that we decided to employ the extrafascial apicolysis of Semb<sup>1</sup> with the hope that it would in part offer a solution to this problem.

In 1932 Semb<sup>1</sup> first attempted to solve these difficulties. Although numerous types of apicolysis had been suggested and tried with a fair degree of success, it became evident to him that they were inadequate because of their failure to accomplish their purpose. He found that

<sup>1</sup>Received for publication, July 31, 1937.

the entire apex could be mobilized extrafascially by its separation from three groups of suspensory ligaments. This allowed the apex and surrounding soft tissues to drop downward toward the hilum where they would remain in a collapsed and relaxed condition until the periosteum regenerated new bone. The accompanying rib resections added the necessary lateral collapse. It had another advantage in that it permitted a selective apical collapse. Since the great majority of cavities occur at the apex, it was no longer necessary to sacrifice the lower healthy lung through extensive rib resection in order

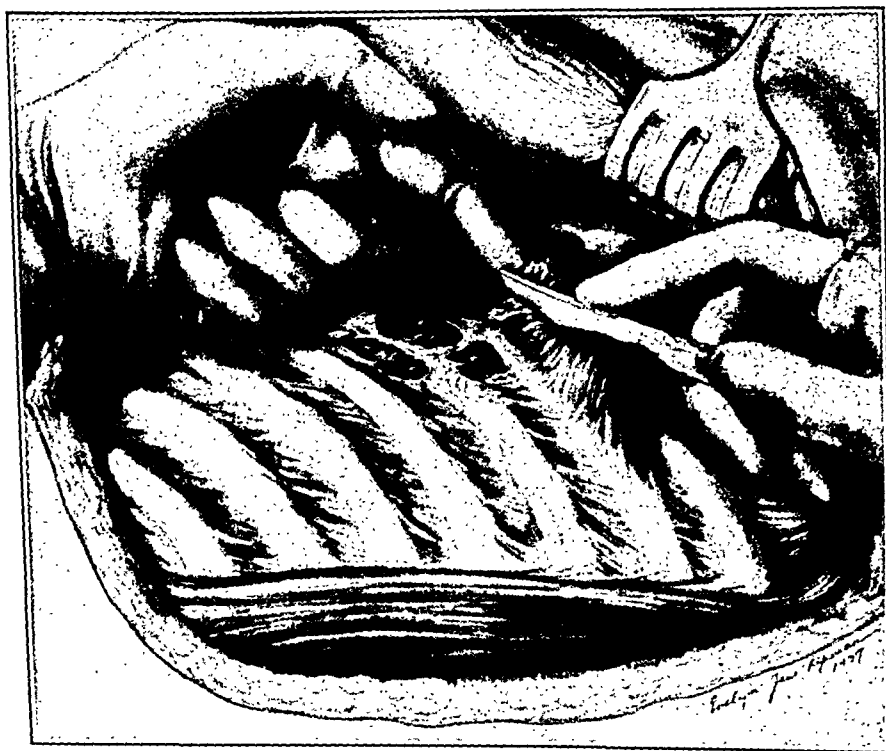


Fig. 1.—Shows the chest wall exposed and the division of the serratus upward from the fourth rib.

to produce closure of the localized cavities. This resulted in the preservation of a higher vital capacity, less dyspnea, and less chronic invalidism.

#### TECHNIQUE

The operation is performed through a paravertebral incision with the patient lying on his side or abdomen, care being taken not to divide the trapezius completely. The scapula is retracted and mobilized by sharp dissection of the insertion of the serratus anterior downward to the level of the fourth rib (Fig. 1). The third, second, and first ribs are resected in order, about two-thirds of the third and almost all of the second and

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hemostat can be placed on the periosteum at the insertion and an excellent exposure of all important structures can be obtained before division of the muscle.

The apicolysis is started by dividing the fibers between the neurovascular trunk and the pleura. This can usually be done with gauze over the finger tips by gentle pressure forward and downward. This site is chosen because the attachment here is frequently loose. Posteriorly there is seen a well-developed fibrous band of varying density (Sebileau's band) extending from the parietal pleura and overlying endothoracic fascia. It passes upward and backward toward the ver-



Fig. 3.—Shows the scoliosis which has taken place following a first stage thoracoplasty with apicolysis and removal of the second, third and fourth transverse processes. This we consider a justifiable reason for preserving the transverse processes. The same degree of collapse is accomplished through removal of the ribs far down on the neck.

tebra covering the first thoracic component of the brachial plexus as it emerges from under the neck of the first rib. This is isolated and cut giving immediate exposure of the nerve trunk. Almost invariably another band is seen lying beneath; that is, medial to the nerve trunk, and this is treated in a like manner. The separation is carried forward to the first rib cartilage and the periosteum divided. As the dissection is carried medially, we find the peripleuritis more marked and sharp dissection may have to be substituted to insure safety. When the first transverse process is reached the dissection is carried



the first around to the cartilage. Posteriorly the transverse processes are not resected but the articulation between the third and second ribs and their respective transverse processes are separated and the ribs divided far down on the neck (Fig. 2). This is very effective in obliterating the costovertebral gutter and at the same time avoids injury to the intertransverse ligaments which may result in a scoliosis (Fig. 3). In certain instances where the cavity lies high in the apex and close to the costovertebral gutter, it is advantageous to disarticulate the first rib and divide it far down on the neck just as in the lower ribs. This gives an unobstructed view of the apex and its accompanying ligaments which insert in the vertebral bodies. The lysis of this area can then be done under direct vision and with less danger of breaking into the underlying cavities. The usual care must be exercised in avoiding injury to the vessels and nerves in removing the first rib. Semb at this point sepa-

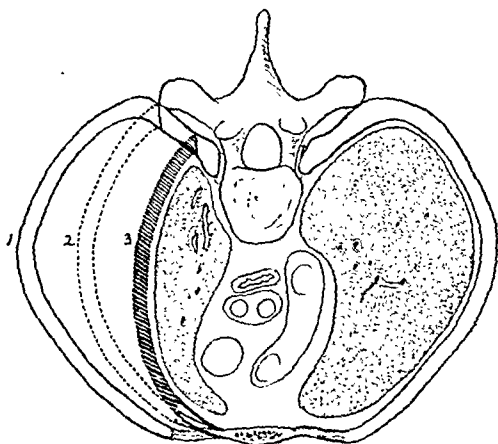


Fig. 2.—Shows a diagrammatic sketch of a transverse section through the thorax. 1 shows the normal contour before resection; 2 shows the contour of the chest after removal of rib segments to the transverse process; and 3 shows the marked reduction of the anteroposterior and transverse diameters of the chest wall when the resections are carried far down on the neck of the ribs.

rates the periosteum of the first rib posteriorly and forward to the attachment of the scalenus anticus muscle. He divides the rib at the transverse process, and with a bone-holding forceps traction is exerted downward and backward exposing the insertion of the scalenus anticus muscle, which can be divided outside the periosteum. The remainder of the rib is then removed to the cartilage. We have preferred to remove the rib first and then to divide the insertion of the scalenus anticus from the periosteum sacrificing the latter which was attached to the anterior rib margin. Semb's method has one distinct disadvantage. The insertion of the muscle is seen only from the posterior surface and if great care is not employed the brachial plexus or subclavian artery may be injured. If the rib is removed first, a

at the original site of the apex and another in the apex in its lysed position. We have prevented this rise by suturing the posterior ends of the divided periosteum and muscle bundles to the anterior edge of the neck of the first intact rib, usually fourth or fifth, depending on the extent of the resection (Fig. 5*B*). This is followed by one or two sutures to the upper edge of the rib medially and anteriorly. Where possible a suture is placed through the apical pleura drawing it downward to the neck of the first intact rib. This procedure obliterates the costovertebral gutter (Fig. 7*C*), and it has been especially useful in cases with little pleural reaction where paradoxical respiration was marked. Once the sutures are placed, the intercostal bundles form an apical cap covering the lowered apex (Figs. 5*A* and 6*B*). The periosteum remains intact and through regeneration of new bone there is no chance left for the apex to ascend toward its original position by scar tissue contraction. Overholt<sup>2</sup> advocates the removal of the periosteum, intercostal bundles, vessels and nerves of the first and second ribs at the

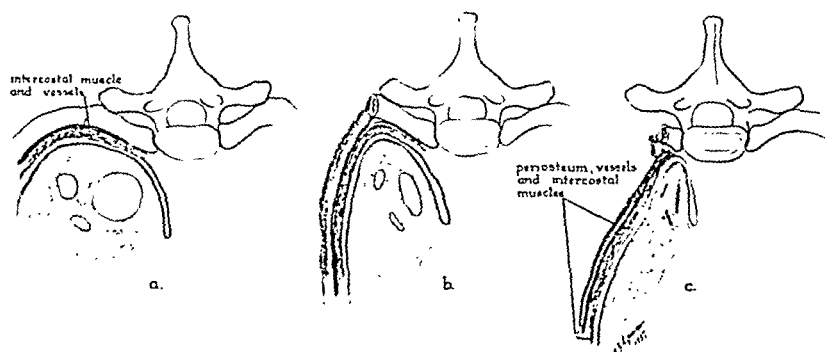


FIG. 7.—*a* shows the normal costovertebral gutter before resection. *b* shows the effect of removal of the rib to the transverse process. *c* shows the effect of disarticulation of the rib and division far down on the neck. Note the increase in antero-posterior and lateral collapse.

time of the apicolysis. We do not find any advantage in this procedure. The preservation of these structures seems advantageous first to form an apical covering which, when sutured, holds the apex in its new position. Second, these structures are frequently firmly attached to the endothoracic fascia as a result of the underlying tuberculous process and to carry out a wide dissection in this area may result in a tuberculous infection of the wound.

Our experiences with the earlier cases in which the bundles were left intact and not sutured showed a definite rise of the apex; therefore, we feel that such a sacrifice of the periosteum would invariably result in a movable apex with paradoxical breathing and retraction toward its original position. Once complete hemostasis is obtained, the wound is closed by muscle approximation with 1-20-day catgut. Drainage may or may not be instituted. We have had better results

level, we encountered an occasional patient where the separation medially was impossible. The dissection is usually very easy on the anterior surface since most cavities lie medially or posteriorly. Anteriorly the pleura is very thin and is easily torn. The internal mammary vessels can be seen and should not be injured. The extent of the apicolysis will be determined by the preoperative condition of the patient, the location and nature of the underlying pathology, the amount of paradoxical breathing, the reaction of the patient to the anesthetic, and the extent of rib resection. In our earlier cases we removed all of the first three ribs around to their cartilages. This was accompanied by marked reactions. Through the suggestion of Semb we changed to a removal of all of only the first rib, less of the

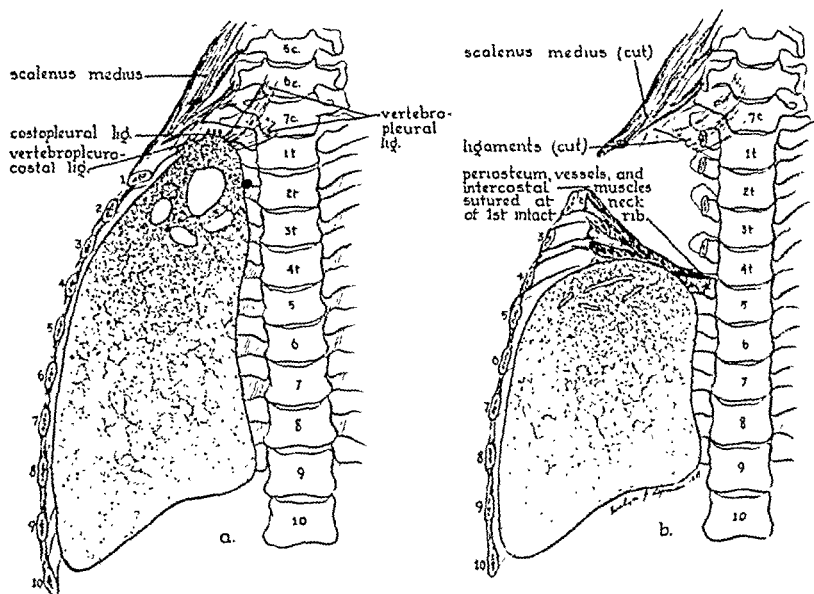


Fig. 6.—*a* shows a diagrammatic sketch of apical structures which must be divided to insure a complete apicolysis. *b* shows the appearance of the lung after apicolysis and fixation of the apex in its new position.

second, and still less of the third and fourth. We then merely uncapped the pleural cupola, at the same time leaving the anterior segments of the second, third and fourth ribs as a support to the anterior portion of the lung. (Fig. 4A.) This permitted much less paradox and was accompanied by less shock. The removal of the anterior segments at a later second stage adds the necessary lateral collapse. It is best to err on the conservative rather than on the radical side. Once the apicolysis is complete, Semb closes the wound. We have felt that there was no assurance that the apex would remain in the collapsed position. In our early cases we noted a tendency for the apex to rise an interspace or more within the first four weeks after operation. This was very easily demonstrated by placing a silver clip

thereby providing a certain degree of relaxation and collapse. This is a radical procedure in itself and the lateral collapse through the removal of the anterior rib segments should not be added until a later date. Our experience with this group of cases has shown that the second stage should not be attempted in less than three weeks, preferably four.

As a rule an incision is made through the old scar, but not throughout its entire extent. No effort is made to examine the apex, but instead care is exercised to avoid the opening of the serous cavity which has acted as an efficient tamponade since the previous apicolysis. If the apicolysis is to be increased at this stage, it is necessary to evacuate the cavity in order to divide the intercostal bundle and periosteum of the first intact rib. The anterior segments of the third and fourth ribs are divided anteriorly but not necessarily around to the cartilages. This should be left to another stage. It is not unusual for the cavity which persists to appear as a transverse slit at the site of the first (usually fifth) intact rib near the costovertebral gutter. It is therefore more important to remove the posterior segments of the intact ribs than all of the anterior segments of the ribs above. The extent of the resections will depend on several factors; i.e., the nature of the lesion, its size and location, the reaction of the patient to the first stage, his vital capacity, blood picture, and sedimentation rate. Where these are satisfactory, it has been a practice to remove the necessary length of the fifth, sixth, and seventh ribs. It is definitely advantageous to get a segment of the seventh to prevent an incarceration of the scapula and to remove all possible barriers which might prevent it from falling into the collapsed chest wall. Every patient is treated as an individual problem and it may be found necessary to add a third and even fourth stage operation if his condition will not permit the necessary amount of rib removal at the second stage.

#### ANTEROLATERAL STAGE

With large upper lobe stiff-walled cavities it is necessary to remove all of the anterior segments of the upper four or five ribs. This operation is done as a third stage and removes all support from the anterolateral chest wall, thereby insuring the maximum collapse through the proper usage of shot bags and pressure pads. The incision employed is along the lateral border of the pectoral muscle on women, but on men we use a vertical parasternal incision extending from the first rib cartilage downward as far as necessary. The fibers of the pectoralis major are separated and the cartilages and the remaining anterior rib segments are removed flush with the sternum. The first rib cartilage is not disturbed. Its removal has not been found necessary since at the time of the apicolysis the periosteum of the first rib

without it. This will be discussed later. Semb<sup>1</sup> prefers a catheter drainage for forty-eight hours with frequent aspirations. In certain instances this has definite advantages since there is an excess of serum which forms in the large dead space left remaining (Fig. 8). We have yet to see a single instance where serum accumulation has not occurred. Because of this we have not found it necessary to fill the dead space above the apex with saline solution as advocated by Overholt.<sup>2</sup> If drainage is instituted, the catheter can be connected to a negative pressure apparatus or kept empty by frequent aspirations during the first forty-eight hours. The constant suction is probably better since it permits less meddling and therefore lessens the chance of introducing infection. The apex is fixed by sutures and there is



Fig. 8.—A, x-ray film of chest showing large apical cavity on the right side; the right hemidiaphragm is not paralyzed. B, same patient after operation; there is no evidence of atelectasis. The homogeneous density above is due to a collection of serum in the dead space formed by the lysis of the apex. 1 shows original site of apex; 2 shows the site of the apex after apicolysis.

no danger of its returning to its former position. The average time consumed for the entire operation, once the operator is familiar with the technique, is three-fourths to one hour. Any attempt to shatter records will only result in needless trauma, injury to important structures, and unnecessary complications.

#### THE SECOND STAGE

In most instances where the cavities have been large and surrounded by thick fibrous tissue walls, a second stage operation has been indicated. We do not feel that this is any argument against apicolysis since the first stage, depending upon the extent of the lysis, cannot be expected to do more than shorten the longitudinal axis of the lung,

the same as is done in a first stage apicolysis. These sutures serve the same purpose; namely, preventing a rise of the apex to its former position during healing. The wound is then closed without drainage. The revision operation is much more tedious than the primary one because of the disturbed anatomic relations. It, therefore, requires one to two hours operating time. From our limited experience, it has been found that revision operations are next to technically impossible if nine to twelve months have not elapsed following the primary stage. This allows sufficient time for the regenerated ribs to become thoroughly calcified. Before this, the incompletely regenerated periosteum is fibrous and cannot be separated. The only recourse then is its removal, which sacrifices the one possible chance for a rigid support of the underlying collapsed lung.

#### POSTOPERATIVE CARE

The care of the patient following apicolysis is most important since the procedure is accompanied by more shock than following an ordinary first stage thoracoplasty. This occurs as the result of a combination of several factors. The patient has been submitted to a more radical procedure entailing a much wider dissection with a disturbance of normal physiologic relations. The wound is exposed for a longer period and the blood loss is greater. All of our patients suffered from shock following operation. The intensity ranged from a mild to a severe degree. Our criteria for shock are based on a low blood pressure, systolic below 85 mm. Hg. accompanied by a rapid pulse, over 100, and a pale, cold, leaky skin. We have attempted to prevent this by the administration of rectal and intravenous fluids during the operation. The first evidence of shock often manifests itself when the patient is transferred from the operating table to his bed. This occurs whether the operation has been performed in the prone or lateral position. We have always placed the patients on the bed in the supine position since there is less pain and the respiratory exchange is most efficient in this position. Intrapharyngeal oxygen is used routinely after each first stage. The nasal tube is inserted by the anesthetist while the patient is on the operating table; the oxygen flow is regulated between five and seven liters per minute. This is continued for the first twenty-four to forty-eight hours after which it is gradually reduced until the patient is weaned. If the degree of shock is marked, heat is applied through the use of an electric cradle. Intravenous glucose and subcutaneous saline are administered first. If these do not succeed in maintaining the blood pressure, a transfusion is given. The patient's position is frequently changed and we insist on his coughing to rid the tracheobronchial tree of any secretions which may have been squeezed from the cavity during the lysis. This is important particularly in cases where the diaphragm on the

was divided anteriorly and allowed to follow downward with the apex. It therefore offers no barrier to collapse. This saves time since its removal is more difficult than the other cartilages.

#### REVISION OPERATIONS

It is generally accepted that there are certain cavities which will resist all the collapse measures which we have available. There are a small number of these if we make a critical analysis of our failures. The usual causes are: the removal of an inadequate amount of rib in the region of the cavity, too few stages, or the inefficient use of pressure pads. We have encountered several of these patients and realized that further surgery was needed. The cases chosen were those who had had adequate rib removed but in whom cavity closure was unsuccessful because the cavity had been converted from a rounded one into a narrow longitudinal slit nestling in the costovertebral gutter alongside the bodies of the upper three or four dorsal vertebrae. In this series it was obvious that the maximum amount of pressure applied laterally had been obtained and that the cavity was suspended from the apex due to its fixation through ligamentous attachments. To overcome this and to promote longitudinal collapse, a paravertebral incision is made through the old scar. The scapula is separated from the chest wall by sharp dissection. Since there is a distortion of the normal anatomic relations, especially in the region of the brachial plexus and the regenerated first rib, it is much safer to start at the level of the third or fourth ribs near the vertebrae. The regenerated segments are removed until the first rib is reached. At times this will allow adequate orientation to proceed with its removal providing the scalene muscles have not pulled the regenerated periosteum high into the neck. If this condition exists, it is much simpler to start at the level of the fourth rib at its posterior end and find the line of cleavage in the endothoracic fascia. By dividing the intercostal bundles and periosteum, the line of cleavage can be followed upward. The apex is exposed as an elongated cone pointing upward. The greatest care must be exercised as the lysis is carried out since the cavity may be opened resulting in numerous complications (to be discussed later). If a marked peripleuritis is present, the lysis should be done by sharp dissection. When the ligaments at the apex are divided, the operator must be on guard against injury to the first thoracic component of the brachial plexus. It is possible at times to complete the lysis without disturbing the regenerated first rib. If it is left, no barrier to collapse is offered by its presence because the lung containing the lesion will be displaced downward. Removal of the rib is much easier after the lysis has been completed because all important structures can be easily visualized. At this stage we suture the posterior ends of the divided intercostal bundles and periosteum to the first intact rib

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peripheral or spinal block anesthesia, chloroform, or tribromethanol are used. Certain unsatisfactory accompaniments with the usage of the latter group, such as prolonged circulatory and respiratory depression, have seemed to us to overshadow the few possible advantages they may possess.

Moderate premedication with morphine and scopolamine followed by skillful, quiet induction of the anesthesia by inhalation has, in our hands, seldom resulted in disturbances of respiration. The use of the carbon dioxide absorption technique has proved desirable since it offers the patient a warm, moist atmosphere. Absolute freedom from respiratory obstruction is essential, and with few exceptions we have found a pharyngeal airway adequate. This permits a lighter plane of anesthesia than is required for tracheal intubation. A slow induction with nitrous oxide or cyclopropane with a small face mask affords little dead space. An atmosphere is employed which simulates the oxygen content of room air as closely as is consistent with adequate oxygenation of the blood and tissues. This will, in a majority of cases, produce anesthesia without cough or hyperpnea.

Certain precautions in the application of carbon dioxide absorption technique are important. We believe that a minimum disturbance of the oxygen and carbon dioxide balance of the patient's blood and tissues gives the best results. Oxygen tension in the anesthetic atmosphere, in excess of that sufficient to avoid bad color and disturbances of the pulse rate and blood pressure, has at times seemed to give a false sense of security during the operation and has been followed by disappointment in the immediate postoperative period. Physical control of intrapulmonary pressure by moderate and carefully individualized distention of the thin rubber breathing bag will usually control any tendency to paradoxical respiration.

#### ANALYSIS OF CASES

This report consists of an analysis of sixty-five cases which have had extrafascial apicolysis. Forty-four of these have been operated upon at the Wisconsin General Hospital and twenty-one at the Wisconsin State Sanatorium during an eighteen-month period from January, 1936, to July, 1937. Eight additional cases have undergone revision operations with extrafascial apicolysis.

#### INDICATIONS FOR OPERATION

Our indications for this procedure on the sixty-five primary cases have been rather broad. We have used it with apical cavitation, particularly in large single or multiple cavities surrounded by thick inelastic fibrous tissue walls and atelectatic indurated lung parenchyma. It was also used when the disease was confined to the apex since it permitted the preservation of the uninvolved portion of the lung. Except

operated side is fixed. Unless these secretions are removed, an atelectasis may result. The usual drugs are employed to control pain. These are used in as small doses as possible in order not to suppress the cough reflex. A bedside x-ray film is taken during the first twenty-four hours to determine if any atelectasis has occurred. This is followed by more films to provide a close check on any important change in the pulmonary pathology which may manifest itself later. Compression pads are used as soon as they can be tolerated by the patient. The wound is watched closely for evidence of increased pressure within the dead space. This manifests itself in the form of a quickened respiratory rate, pain in the arm on the operated side, and at times by a bulging at the base of the neck anteriorly. If the pressure is sufficient to cause these signs and symptoms, a needle is inserted in the interscapular space at a distance from the line of incision and the excess serum removed. This is always cultured to determine the presence or absence of microorganisms. The pain following apicolysis is less than that encountered following ordinary thoracoplasty. This is probably due to the division of the upper intercostal nerves. The postoperative care following the second or anterolateral stages is essentially the same as following the first stage. These, however, are accompanied by less shock and discomfort. The blood picture should be checked closely following each stage since the cumulative effect of previous stages often lowers the hemoglobin remarkably. This is controlled with frequent small blood transfusions.

#### ANESTHESIA

The problem of anesthesia for these patients is a complicated one. A mutual understanding between the surgeon and the anesthetist is imperative. Waters and his staff have cooperated with us in solving these difficulties and this has resulted in the evolution of a technique which is satisfactory for the patient as well as the anesthetist and the surgeon. Waters<sup>3</sup> feels that an acquaintance with the use of a given combination of drugs and a certain skill in the individualization of their administration is most important. He states that no one agent or technique solves the problem for all patients or for every surgeon or anesthetist. Coughing, hyperpnea, and paradoxical breathing are to be avoided since they not only increase the difficulty of the surgical procedure but also increase the liability of the spread of infected secretions into clean areas of the tracheobronchial tree and possible rupture of the lung. Excessive bleeding is to be avoided. A depression of the cough reflex for a period longer than the time consumed for the operation is undesirable.

All of the following gases: nitrous oxide, ethylene, cyclopropane, and ether in moderate dosage probably increase peripheral blood flow. This results in a greater loss of blood during the operation than when

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TABLE II  
CAUSES OF COMPLICATIONS WHICH WERE "UNPREDICTABLE"

NO. OF PATIENTS	CAUSE	OUTCOME
4	Severe wound infection	Recovered
1	Streptococcus pneumonia	Died
1	Hemorrhage after cavity was opened at time of operation	Died
1	Cystitis and bilateral phlebitis	Recovered
1	Cardiac dilatation	Died
1	Diabetes and severe wound infection	Still in hospital
1	Tuberculous empyema	Recovered
1	Pulmonary thrombosis	Died
1	Heart failure (digitalis)	Recovered
1	Wound infection and asthma	Recovered
13 Total		Dead, 4 Recovered, 8 Still in hospital, 1

room if they had an upper respiratory infection. Only those actively engaged in the operation were allowed in the operating room. These precautions resulted in a marked reduction in the number of infections, but did not succeed in entirely eradicating them. Our attention was then directed to the fact that a much higher percentage of infections occurred in the patients in whom drainage was instituted. For this reason we have now eliminated all drainage following apicolysis with the result that we are getting an increasingly small number of infections.

TABLE III  
RELATIONSHIP OF INFECTION TO DRAINAGE

NO. OF STAGES		CLEAN	INFECTED
<i>A</i>			
30	One stage with apicolysis drained	23	7 (23.0%)
35	One stage with apicolysis not drained	32	3 ( 8.5%)
65	Total	55	10 (15.0%)
<i>B</i>			
26	Second, third and anterolateral stages drained	22	4 (15.4%)
49	Second, third and anterolateral stages not drained	47	2 ( 4.0%)
75	Total	69	6 ( 8.0%)
<i>A and B</i>			
56	Drained	45	11 (19.6%)
84	Not drained	79	5 ( 5.9%)
140	Total*	124	16 (11.4%)

\*Ten operations that were done through previously infected fields are not shown in this table.

*Causes of Complications Which Were Predictable (See Table IV).—*Certain complications can be avoided if due care and diligence are exercised in the choice of cases for surgery. These we have called predictable since in the majority of instances their occurrence could have been greatly reduced or entirely avoided if sufficient significance had been attached to the laboratory and clinical data at hand pre-

in one instance, we have not employed the procedure where apical cavities were not demonstrable because the added hazard was not deemed justifiable. There were certain clinical, laboratory, and x-ray findings which were found to be of some prognostic significance. These have been correlated with the convalescence which has been divided into three types: First, *the easy* in which there was no more than the ordinary postoperative febrile reaction on the second and third days, little or no dyspnea, no increased toxemia, and no necessity for postponement of the second stage. Second, *the moderately severe* in which there was a short-lived dyspnea, transient increase in toxemia during the first week after operation, and where it was necessary to delay the second stage for a period of not over six weeks. Third, *the stormy* where there was a severe and prolonged postoperative febrile reaction, moderate to severe dyspnea requiring oxygen for at least one week or more after operation, marked toxemia with or without x-ray evidence of a spread of the tuberculous process, and where the second stage had to be delayed for a period of six weeks to six months.

*Cause of Death in Sixty-Five Patients (See Table I).*—The argument often used against the performance of a given surgical operation is frequently directed at the accompanying mortality. This was one of the chief early objections to extrapleural thoracoplasty. It has been practically dispelled, however, with an increasing experience which has taught us to fit the operation to the patient and not the patient to the operation. This attitude will, we believe, enable us to continue to reduce the mortality following this more radical procedure.

TABLE I  
CAUSE OF DEATH IN SIXTY-FIVE CASES

AGE AND SEX	CAUSE	POSTOPERATIVE DAY
39 M	Cardiac dilatation	1
29 M	Streptococcus pneumonia	8
42 M	Tuberculous wound infection and hemorrhage	60
31 F	Pulmonary thrombosis	6
37 F	Tuberculous pneumonia on opposite side	6
7.6% Total mortality		

*Causes of Complications Which Were Unpredictable (See Table II).*—Certain unpredictable complications will always occur in cases of this type. Although they may not always be of a serious nature, they are usually the cause of a fair percentage of the deaths.

*Relationship of Infection to Drainage (See Table III).*—After performing several of these operations it soon became evident that we were getting an extraordinarily high percentage of infections. At the time there were a large number of acute respiratory infections among our operating room staff. We attempted to eliminate this source of contamination by excluding all assistants and nurses from the operating

toxemia and often pain over the collapsed area. The temperature was usually slightly elevated; dyspnea and cyanosis appeared particularly in those patients with a low vital capacity. The lung field became opaque to x-ray (Fig. 9B). The sputum, which was temporarily increased after operation, diminished greatly or became absent. On physical examination the heart could be found to have shifted to the collapsed side, depending upon the flexibility of the mediastinum. The percussion note was dull to flat. Breath sounds were greatly diminished to absent; if present, usually bronchial in character and heard only over the hilum. If the collapse was uncomplicated by a spread of the tuberculous process or infection, it gradually cleared over a period of two to three weeks. X-rays showed the density clearing at the hilum and in the larger bronchi first. This was accompanied by the appearance of râles here. The sputum which was scanty or entirely absent became copious for the next two to three days. The patient's general condition improved, the appetite increased, and the pulse and temperature returned to normal. Usually the lung entirely cleared in three to four weeks (Fig. 10).

From these figures we assume that preoperative diaphragmatic paralysis was a factor in the production of a postoperative atelectasis. The mechanics are not thoroughly understood. Theoretically it may be said that the pistonlike action of the diaphragm is a most important asset in keeping the bronchial passages free of secretions. If this action is lost, the overactivity of the unopposed intercostal muscles is inadequate. This may be true in a certain group of cases, but does not answer the question satisfactorily since 26.5 per cent of those with normal diaphragmatic movement were victims of the same complication. Some of these patients may have developed this condition because of a stenosed bronchus or through the aspiration of a large amount of thick tenacious material which could not be expelled under any conditions. Another factor conducive to the development of subsequent atelectasis is the weakening of the chest wall through rib resection and paradoxical respiration. These we have tried to eliminate by the removal of shorter segments of the fourth, third, and second ribs at the time of the apicolysis. The paradoxical respiration has further been combatted by suturing the apex and surrounding structures in their new position (see Technique). This complication has occurred in both groups despite a careful preoperative emptying of the tracheobronchial tree by coughing and light anesthesia during the operation which will allow cough immediately after. We are unable to say at this time whether this condition occurs more frequently after apicolysis than after an ordinary first stage thoracoplasty.

*Relationship of Atelectasis to Postoperative Convalescence (See Table VI).*—The question of postoperative atelectasis is debatable since certain authors have failed to recognize it as a complication. Others feel



operatively. On the other hand, it must be remembered that the bad risk patient is doomed to chronic invalidism or early death if surgical collapse is not instituted. The number of operative stages will have to be increased and each stage lessened in extent, often being accompanied by a predictable stormy convalescence or even death. Regardless of this, it seems justifiable to attempt to salvage what few we can from a certain fatal outcome.

TABLE IV  
CAUSES OF COMPLICATIONS WHICH WERE "PREDICTABLE"

NO. OF PATIENTS HAVING A STORMY COURSE	
2	Spread of tuberculous process to opposite side (one dead)
6	Prolonged atelectasis with questionable tuberculous pneumonia
4	Tuberculous toxemia
1	Atelectasis and spread of tuberculous process to the base
1	Spread of tuberculosis to both sides
1	Tuberculous pneumonia
15	Total

*The Relationship of Diaphragmatic Paralysis and Postoperative Atelectasis (See Table V).*—A study was made of forty-four patients.\* All were fluoroscoped to determine if there was a true diaphragmatic paralysis present. In one instance the paralysis was questionable because of a thickened pleura and accompanying fibrosis of the underlying lung. Two with and five without diaphragmatic paralysis had preoperative atelectasis and two others with questionable paralysis also had preoperative atelectasis. These were not used in our calculations. Of the thirty-five patients in which we were sure as to the mobility of the diaphragm, postoperative atelectasis was almost twice as frequent in the cases with preoperative diaphragmatic paralysis.

TABLE V  
RELATIONSHIP OF DIAPHRAGMATIC PARALYSIS TO POSTOPERATIVE ATELECTASIS

NO. OF PATIENTS	DEVELOPED ATELECTASIS		PER CENT AFTER FIRST STAGE
	AFTER FIRST STAGE	AFTER SECOND STAGE	
16 with diaphragmatic paralysis	8	1	50.0
19 without diaphragmatic paralysis	5	1	26.5
1 with questionable diaphragmatic paralysis		1	
2 with diaphragmatic paralysis with complete preoperative atelectasis			
5 without diaphragmatic paralysis with complete preoperative atelectasis			
1 with questionable diaphragmatic paralysis with complete preoperative atelectasis			
44 Total			

The first signs and symptoms of atelectasis usually occurred on the third or fourth postoperative day. There were signs of increased

\*Only forty-four of these cases were considered since the remaining twenty-one were done in the Wisconsin State Sanatorium where it was impossible to obtain routine bedside x-rays postoperatively.

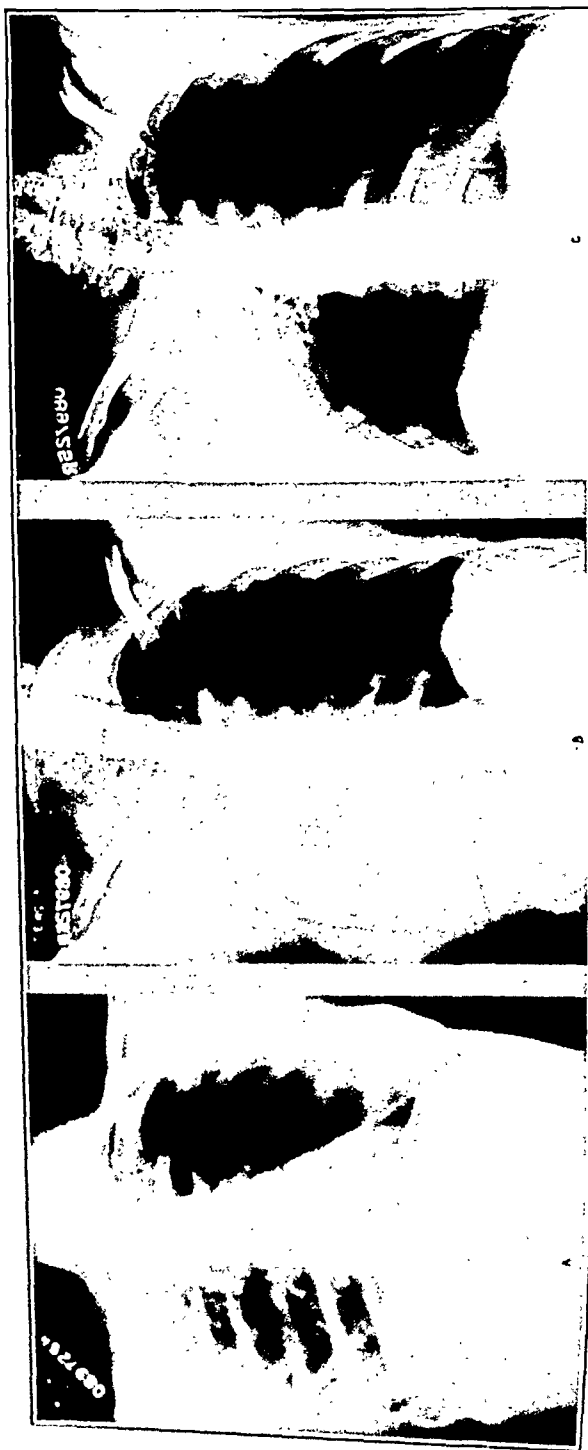


Fig. 10.—A, X-ray of chest showing right upper lobe cavity with fibrosis. B, shows the development of atelectasis throughout the operated lung. C, shows complete clearing of uncollapsed portion of the lung three weeks after operation. This patient had a moderately stormy post-operative course necessitating delay of the second stage operation.

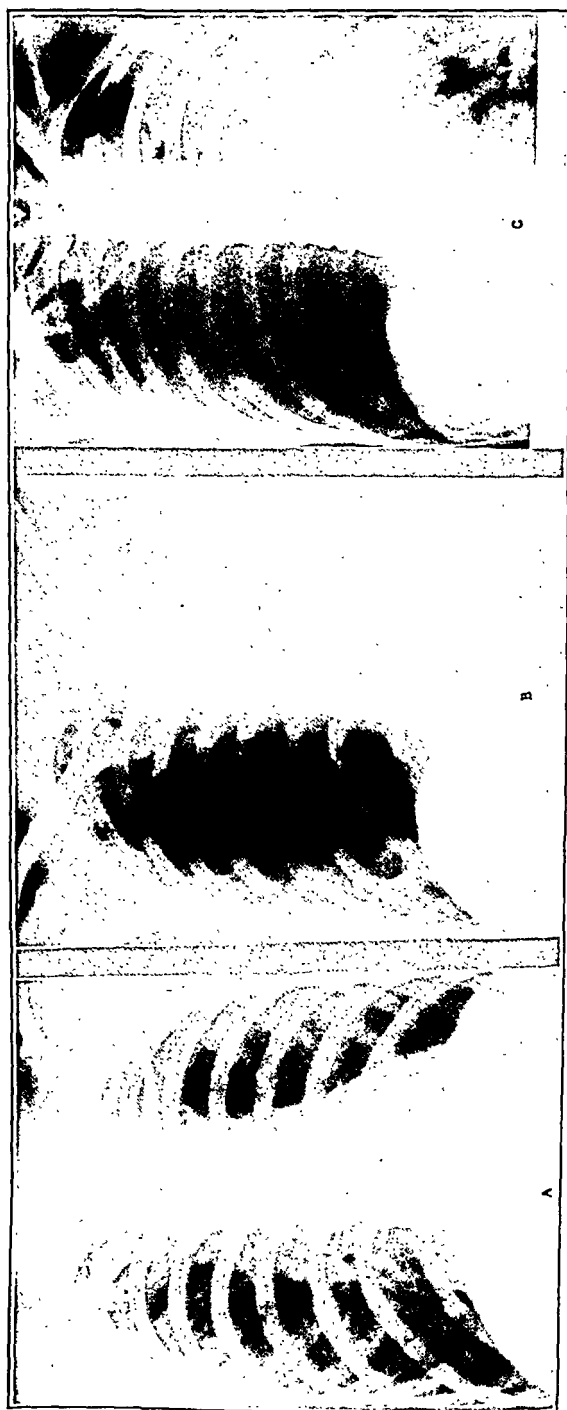


Fig. 9.—A, x-ray film of chest showing large apical cavity on the left; the left hemidiaphragm has been paralyzed. B, same patient forty-eight hours after operation. Note homogeneous density throughout the left lung field due to atelectasis. C, same patient two weeks later. The lung field is clearing; the density disappears as the lung becomes aerated. The rarched area above simulating a cavity is due to air trapped in the dead space above the apex.

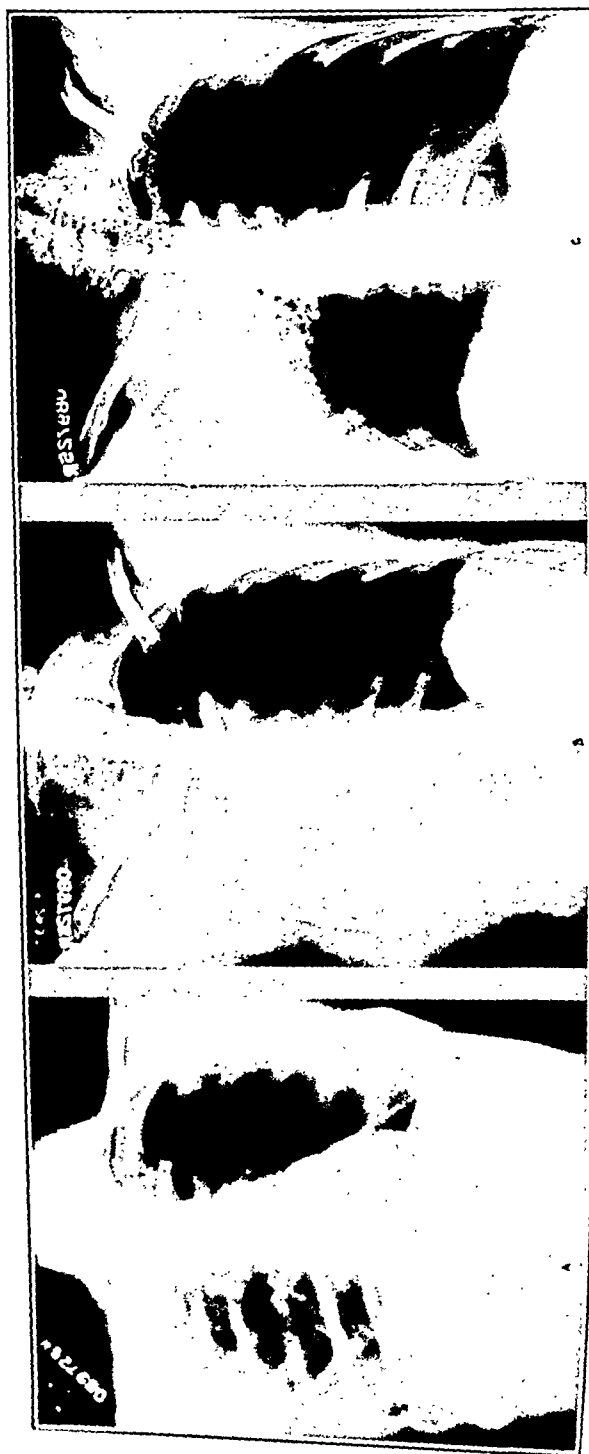


Fig. 10.—A, X-ray of chest showing right upper lobe cavity with fibrosis. B, shows the development of atelectasis throughout the operated lung. C, shows complete clearing of collapsed portion of the lung three weeks after operation. This patient had a moderately stormy post-operative course necessitating delay of the second stage operation.

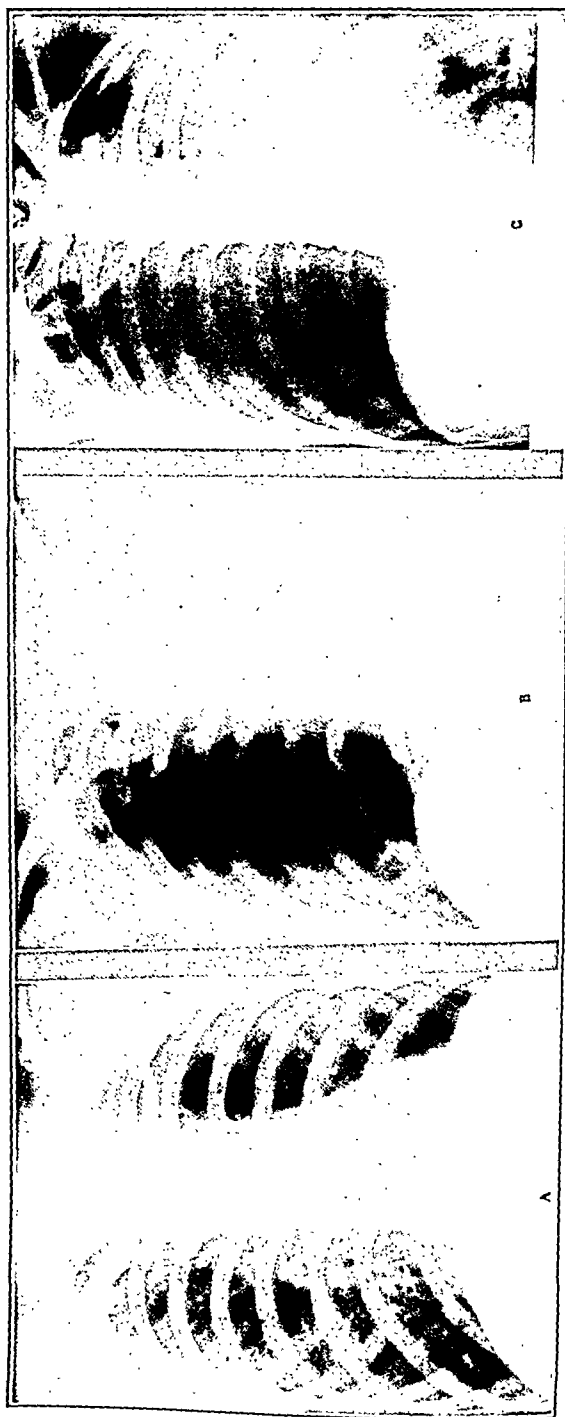


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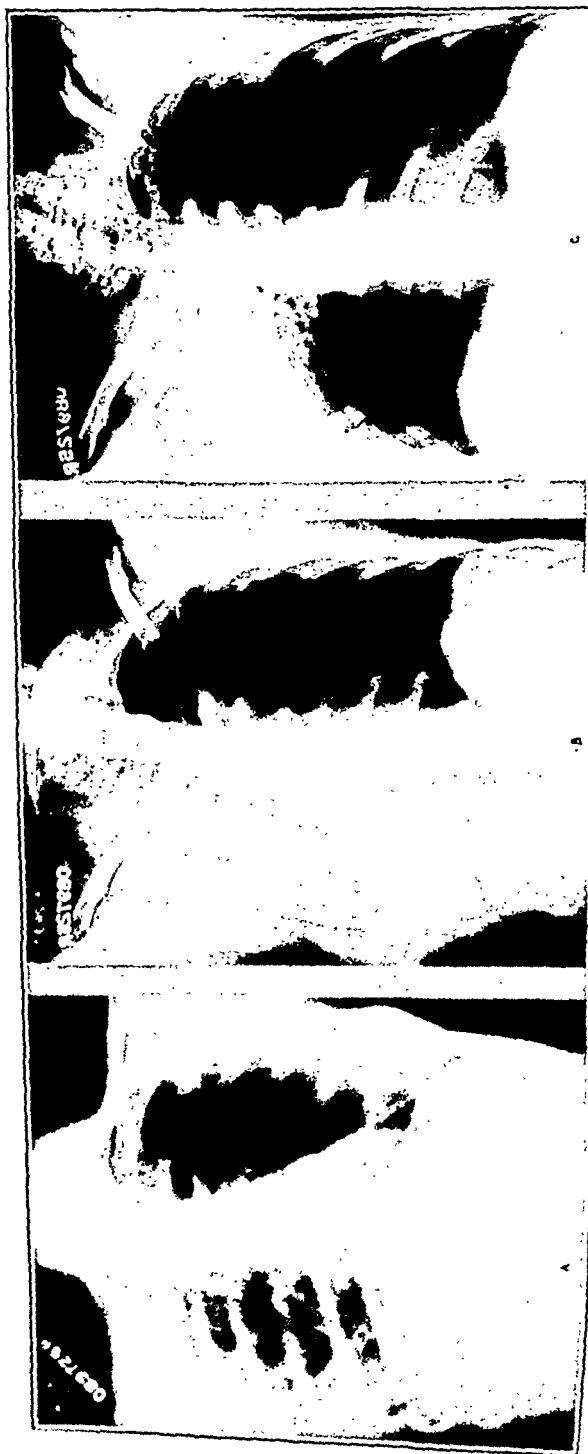


FIG. 10.—A, X-ray of chest showing right upper lobe cavity with fibrosis. B, shows the development of atelectasis throughout the operated lung. C, shows complete clearing of uncollapsed portion of the lung three weeks after operation. This patient had a moderately stormy post-operative course necessitating delay of the second stage operation.

that it is rare and that what is called atelectasis is nothing more than a so-called pleural reaction. To check this we have made many thoracenteses to determine if a pleural exudate was present and in every instance no fluid was obtained. After following these cases carefully by physical examination and x-ray, we noted a clearing of the lung parenchyma in most instances. Because of our experience we feel that the cause of a stormy convalescence is frequently misunderstood and the etiology erroneously attributed to an autotuberculinization, spread of the tuberculous process, or to a tuberculous pneumonia, when in reality it is due to an atelectasis. This complication very frequently produces a stormy postoperative course.

TABLE VI  
RELATIONSHIP OF ATELECTASIS TO POSTOPERATIVE CONVALESCENCE

NO. OF PATIENTS		TYPE OF CONVALESCENCE	
		EASY	STORMY
13*	developed postoperative atelectasis	3	10 (77.0%)
19	did not develop postoperative atelectasis	18	1 ( 5.5%)
7	had preoperative atelectasis	4	3 (43.0%)
39	Total	25	14 (36.0%)

\*Of these 13 patients, 8 (62%) had preoperative diaphragmatic paralysis. Five were taken out because they had unpredictable complications.

*The Effect of Active Progressive Contralateral Tuberculosis on Convalescence (See Table VII).*—The evaluation of patients who are possible candidates for thoracoplasty is not always easy since frequently the picture is complicated by the presence of contralateral disease. We are unable to predict what the lesion in the opposite lung will do after surgery for closure of the original focus. The shock of the operation along with the temporary lowering of the patient's resistance and the increased burden thrown upon the better lung may result in a rapid spread of the disease. The more acute and widespread the disease in the better lung, the more often this will occur.

TABLE VII  
EFFECT OF ACTIVE PROGRESSIVE CONTRALATERAL TUBERCULOSIS ON CONVALESCENCE

NO. OF PATIENTS		TYPE OF CONVALESCENCE	
		EASY	STORMY
6	with active contralateral tuberculosis	2	4 (67%)
45	with quiescent or no contralateral tuberculosis	34	11 (24%)
1	with questionable contralateral tuberculosis	1	
52	Total	37	15 (36%)

*Showing the Effect of Vital Capacity on Postoperative Course (See Table VIII).*—Since the vital capacity was taken routinely on all patients preoperatively, we have compared these findings with the type of convalescence. In each instance a spirometer was used. The percentage

of normal was calculated for each patient. This was done because the measurement of volume alone is unsatisfactory. A vital capacity of 1 liter for one individual might be 50 per cent of the normal, while in another it would be only 25 per cent of the normal. For several years we have considered a vital capacity of less than 35 per cent as significant of a dangerously low respiratory reserve. We have tried to overcome the associated dangers by doing less at each operation and by increasing the number of stages. We have also realized that many factors must be considered in evaluating the vital capacity readings. If all these factors are kept in mind, we feel that vital capacity readings are of definite value.

TABLE VIII

SHOWING THE EFFECT OF VITAL CAPACITY ON POSTOPERATIVE COURSE

NO. OF PATIENTS	TYPES OF CONVALESCENCE	
	EASY	MODERATELY STORMY OR STORMY
11 vital capacity less than 35%	5 (45%)	6 (55%)
39 vital capacity over 35%	31 (80%)	8 (20%)
2 vital capacity not recorded	1	1
52 Total	37 (72%)	15 (29%)

*Effect of Sedimentation Rate on Convalescence (See Table IX).—*The blood sedimentation rates were checked on these patients and they were classified into three groups: those with a fall of 0 to 15 mm. in one hour *slow*, 15 to 24 mm. *medium*, and over 25 mm. *rapid*. These were in turn compared with the type of convalescence to determine if there might be any possible connection. This comparison shows that the slower the sedimentation rate, the more likely the patient is to have an easy convalescence. It also demonstrates that some importance should be attached to this laboratory procedure.

TABLE IX

EFFECT OF PREOPERATIVE SEDIMENTATION RATE ON CONVALESCENCE

NO. OF PATIENTS	SEDIMENTATION RATE	TYPE OF CONVALESCENCE	
		EASY	MODERATELY STORMY OR STORMY
16	Rapid	9	8 (47%)
22	Medium	17	5 (23%)
15	Slow	11	2 (15%)
52 Total		37	15 (29%)

*The Relationship of the Leucocytic Picture to the Postoperative Convalescence (See Table X).—*A careful record was kept of the preoperative leucocyte counts. This was made as simple as possible since the monocytes were not always counted. If the polymorphonuclears were over 70 per cent and the lymphocytes below 20 per cent, the picture was considered bad. When the polymorphonuclears were above 70



per cent and the lymphocytes above 20 per cent, or the polymorphonuclears below 70 per cent and the lymphocytes below 20 per cent, it was considered fair. If the polymorphonuclears were below 70 per cent and the lymphocytes above 20 per cent, it was considered good. Although this has not been accepted as a classification, we have checked it against the type of convalescence and found that it worked out as expected. We hope to use it in the future as a relatively simple method which will help evaluate the condition of the patient.

TABLE X

RELATIONSHIP OF THE LEUCOCYTIC PICTURE TO THE POSTOPERATIVE CONVALESCENCE

NO. OF PATIENTS	LEUCOCYTIC PICTURE	TYPE OF CONVALESCENCE	
		EASY	STORMY
9	Bad	2	7 (78%)
15	Fair	12	3 (20%)
28	Good	23	5 (18%)
52 Total		37	15 (29%)

*The Effect of Operation on Cavity Closure (See Table XI).*—X-ray films were taken after each operation to determine the effect of each stage on the reduction in size of the cavity. It was evident from these studies that the apicolysis alone did not always succeed in closing the cavity. Other stages had to be performed to add the necessary lateral collapse. In many instances cavities appeared closed to the ordinary flat plate but were found to be open following an overexposed Bucky film. As seen in the table, the percentage of cavities closed was high except in those patients where complications arose which prevented further surgery.

TABLE XI

EFFECT OF OPERATION ON CAVITY CLOSURE

NO. OF PATIENTS	
65	Had apicolysis
5	Died
60	Survived
54	Surgery completed or suspended
53	Cavity present before operation
47 (88.7%)	Cavity closed
6* (11.3%)	Cavity open

\*3 too ill for completion of the contemplated number of stages.

1 had apical cavity closed but basal cavity open.

1 cavity open because of delay of later stages due to wound infection.

1 cavity was thought to be closed but later x-rays demonstrated that it was still open.

*Relation of Cavity Closure to Sputum (See Table XII).*—The closure of a tuberculous cavity does not mean that the patient is going to show a negative sputum. The walls of the cavity may be brought into apposition but the tubercle bacilli continue to escape through a communicating bronchus. If the bronchus is kinked simultaneously with

the cavity closure, the sputum will become negative. We have seen cavities with thick fibrous walls adequately collapsed but no tendency to heal as shown months later at postmortem. It seems more important that the communicating bronchus become closed in old cavities than in the new ones which are still capable of closing and healing with a sufficient amount of relaxation supplied through operation. In this group of cases the ratio of negative sputum ran very close to the

TABLE XII  
RELATION OF CAVITY CLOSURE TO SPUTUM EXAMINATION

NO. OF PATIENTS	
<i>Before Operation</i>	
53	Cavity present
51	Cavity open, sputum +
<i>After Operation</i>	
41 (80%)	Cavity closed, sputum -
2 (4%)	Cavity closed, sputum -, guinea pig +
1 (2%)	Apical cavity closed, basal cavity open, sputum -
2* (4%)	Cavity closed, sputum +
5† (10%)	Cavity open, sputum +

\*In 1 of these patients the cavity was closed on the operated side, but had an open contralateral cavity; sputum +. The other patient had no demonstrable residual cavity; sputum +.

†In 3 of these patients the surgery was suspended because of their poor condition. In 1 patient surgery was delayed beyond the optimum time because of wound infection.

number of closed cavities. The reasons for failure are enumerated. In a small percentage of cases where this discrepancy cannot be satisfactorily explained, an examination should be made to determine the presence of a tuberculous bronchitis or the possibility of an active contralateral lesion.

#### REVISION OPERATIONS (RESULTS)

Eight patients received revision operations with apicolysis. These were necessary because the primary procedures had failed to close the cavities. The mortality in this group was high. Three patients died directly or indirectly as the result of the operation. In one case the cavity was opened accidentally during the apicolysis. This resulted in a severe mixed infection. The convalescence was stormy from the outset. A grave toxemia associated with a high fever, rapid pulse, and an increasing anemia persisted until death, which occurred at the end of six weeks. Just before death there was a severe hemorrhage from the wound which demanded immediate surgery. Upon exploration the entire dead space above the apex and all of the surrounding structures were involved in a widespread tuberculous infection. An intercostal vessel had been eroded and was responsible for the bleeding. While doing the apicolysis on the second patient, the cavity was accidentally entered. It was sutured and remained closed. The wound healed but the patient died four months later of an advanced

per cent and the lymphocytes above 20 per cent, or the polymorphonuclears below 70 per cent and the lymphocytes below 20 per cent, it was considered fair. If the polymorphonuclears were below 70 per cent and the lymphocytes above 20 per cent, it was considered good. Although this has not been accepted as a classification, we have checked it against the type of convalescence and found that it worked out as expected. We hope to use it in the future as a relatively simple method which will help evaluate the condition of the patient.

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## SUMMARY

This report includes sixty-five cases of thoracoplasty with extrafascial apicolysis (Semb) and eight revision operations. A study of certain preoperative findings was made to determine their value as an aid in the selection of cases for surgery. Since the procedure is rather new, the complications were frequent in the earlier cases. These have been greatly reduced with an increasing experience, a more careful selection of cases and the proper timing of the operative stages. The percentage of cavity closures and sputum conversions has been gratifying. It is too early to make a definite statement as to the final outcome, but it is encouraging to know that an increasing number are already being discharged from the sanatoria as arrested cases. The group of revision operations is too small to evaluate except that the most serious complication to be encountered is the accidental opening of the tuberculous cavity. This is best treated by packing the wound wide open to insure adequate drainage.

We wish to express our appreciation to Dr. E. R. Daniels for his cooperation in compiling the data on the group of patients operated upon at the Wisconsin State Sanatorium.

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myocardial degeneration and spread of the tuberculosis to the opposite lung. A revision operation had been attempted on the third patient six months previously. It had to be suspended because of the shock which followed the partial removal of the regenerated segments. At the time of the second revision these segments were completely removed and an apicolysis started. In one over-enthusiastic attempt to do a very radical apicolysis, the cavity was accidentally opened. This was sutured and the wound closed but the patient never regained consciousness. He developed a hemiplegia presumably from an embolus and died twenty-four hours later. An autopsy was not permitted.

Five patients survived and four enjoyed an easy uncomplicated convalescence. In three the cavity was closed and the sputum became negative. In one patient the cavity was apparently not closed even though it was not visible on x-ray. The sputum was negative on smear but positive on guinea pig inoculation. Further surgery is now being instituted. In the other patient the cavity was accidentally opened at the time of operation. The immediate postoperative course was stormy. At this time the wound is healing satisfactorily and the patient's condition is good; his cavity is not visible; and his sputum is negative.

In our limited experience with revision operations of this type, the results have not been as satisfactory as we have desired. The outstanding and most serious complication has arisen following the accidental opening of the incompletely collapsed cavity. In checking this group we have found that this accident has always occurred after the apex had been freed above and just when we were trying to increase the efficiency of the collapse by separating the medial side of the lung from the third or fourth dorsal vertebrae. Invariably the residual cavity has been found just beneath the visceral pleura and so intimately attached to the vertebral bodies that separating was impossible without tearing the lung. Because of these constant findings we are now content to conclude the separation at this point.

The secondary hemorrhage which occurred in two of these cases was most dramatic and proved that no attempt should be made to close the wound with any kind of tube drainage. If this is done exudate collects within the wound cavity and enhances the spread of the tuberculous process in the surrounding tissues. These wounds should be packed widely with vaseline gauze which will not allow any pooling of the infected exudate. This pack should be changed at least once each day. If this is not done, the patient's temperature immediately rises. Dakin's solution has not been used because of the danger of reopening the sutured cavity. Saline has been found to be useful.

ness the studies of DuBois and Hunt on the opossum and cat.<sup>3</sup> Similarly it may explain why faradically induced spasms of the stomach and duodenum inhibit the flow of bile in the cat but not in man.<sup>4</sup>

On the other hand, the discharge of bile from the human gallbladder is speeded up by the presence of peptic ulcers<sup>5</sup> and markedly retarded by pregnancy.<sup>6</sup> In the latter instance, at least, the evidence is strong that retardation is due to a spasticity of the intrinsic musculature at the end of the common duct, and this view is strengthened by recent observations on the human fetus—where the disposition of muscle is easier to follow; namely, that the ampulla of Vater and its musculature is a retrograding segment<sup>7</sup> and that the most important part of the human sphincter of Oddi is the sphincter choledochus—a band of circular muscle enclosing the common duct just before the latter joins the pancreatic duct.<sup>8</sup>

It would thus seem that the time has come to emphasize both the functional unity of the extrahepatic biliary tract and its species peculiarities, and to recognize that in man, at least, a major rôle is played by the *musculus proprius* of the common bile duct.

—Edward A. Boyden, Ph.D.

Minneapolis, Minn.

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#### The Rôle of the Liver in Thyrotoxicosis

THE BELIEF has long been held that the liver is involved in the course of thyrotoxicosis. The most obvious evidence for such a view is the occasional development of jaundice during so-called thyroid crisis; more commonly, subclinical jaundice can be demonstrated by estimation of the icterus index during exacerbations, spontaneous or postoperative, of thyrotoxicosis. There is much similarity between the terminal stages of severe thyrotoxicosis and of hepatitis in that both are marked by fever, delirium, coma, and loss of vasomotor tone as shown by profuse diaphoresis and falling blood pressure. Findings at autopsy in patients who have died in thyroid crisis are notoriously meager, but focal necrosis appears in the liver and in the heart in so considerable a percentage of cases that it cannot be lightly dismissed. That more significance has not been attached to these pathologic findings is due to the fact that a less pronounced degree of parenchymatous damage, such as cloudy swelling, is

## Editorials

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### The Extrahepatic Biliary Tract as a Functional Unit

THE year just ended has witnessed the publication of several studies dealing with the comparative anatomy and physiology of the gallbladder and the sphincter of Oddi. Among these the article by Schmidt and Ivy<sup>1</sup> is of special interest as presenting, for the first time, an attempt to classify the whole extrahepatic biliary tract of higher vertebrates in terms of functional types. This is no mere rationalization but a synthesis of experimental data from some eighteen species, involving a study of the total output and concentration of hepatic bile, the anatomic capacity of the gallbladder, its concentrating power, and the sphincteric resistance exerted at the choledochoduodenal junction. The four types are characterized as follows:

1. *Gallbladder absent*; large output of dilute hepatic bile; sphincteric resistance low (pocket gopher, rat, pigeon, horse).

2. *Gallbladder of low physiologic capacity*, due to large output of dilute hepatic bile and ability of gallbladder to concentrate bile from only two to six times; sphincteric resistance low to moderate (guinea pig, rabbit, African bush rat).

3. *Gallbladder of high anatomic but low physiologic capacity*, due to the small output of concentrated hepatic bile and the inability of the gallbladder to concentrate it much further; sphincteric resistance moderate (pig, sheep, goat, and cow).

4. *Gallbladder of high physiologic capacity*, having the power to concentrate a relatively concentrated hepatic bile six to ten times; sphincteric resistance high (duck, chicken, striped gopher, mouse, cat, dog, and man).

The above analysis, with its series of steps leading up to high sphincteric resistance in man, thus verifies the importance of clinical studies directly attacking the problem of biliary dyskinesia. Even more, however, it reveals the necessity of discriminating, experimentally, between the resistance offered by the duodenum and that produced by the intrinsic musculature that invests the terminal segment of the bile duct; for, if the choledochoduodenal junction of the species listed in Group 4 be examined histologically, it will be found that the extent to which the musculature of the duodenum envelopes the bile duct is much greater in the cat and dog, for instance, than in man;<sup>2</sup> and that this anatomic relationship undoubtedly retards the rate of emptying in animals—wit-

such speculation is fruitless until dependable methods for the estimation of serum lipase and the effectiveness of deaminization of amino-acids, to name but two indications of liver function, are available. Reports on the excretion of hippuric acid are conflicting and the method of Quick is still open to improvement. Extension and confirmation of this work will, we believe, not only throw new light on the nature of thyrotoxicosis but will prove of immediate practical value in the diagnosis of "borderline" or subclinical thyrotoxicosis and in the better control of thyroid medication.

—Willard Bartlett, Jr., M.D.  
St. Louis, Mo.

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1. Somogyi, M.: Proc. Soc. Exper. Biol. & Med. 32: 538, 1936.
2. Bartlett, W., Jr.: Proc. Soc. Exper. Biol. & Med. 36: 843, 1937.



the anticipated event in most febrile forms of exitus. Again, the not infrequent occurrence of glycosuria in thyrotoxicosis is one of the expressions of impaired glucose tolerance. It has been generally considered to be due to an antagonism between the action of insulin and that of thyroxin; it is an established fact, however, that in diabetics decreased glucose tolerance as an expression of liver damage can be produced by a high fat diet alone and that the carbohydrate tolerance of diabetics is further impaired by the onset of thyrotoxicosis. Finally, the clinical value of high carbohydrate diet and, more dramatically, of glucose solutions given intravenously in severe exacerbations of thyrotoxicosis occurring spontaneously or postoperatively is quite as well established as in other conditions in which liver damage is proved.

More certain evidence of the rôle of the liver in thyrotoxicosis has waited, perforce, upon the development of a test sensitive to only moderate impairment of liver function. Such a test we now have, apparently, in Somogyi's method for quantitative determination of blood amylase.<sup>1</sup> With a margin of experimental error of not over 10 per cent, it is accurate for the estimation of small quantities of the enzyme, which cannot be claimed for other methods. It is the view of Somogyi and his coworkers, based upon several thousand determinations in the past five years, that the production of the enzyme depends upon the liver. It has now been shown that there is a relationship between the level of thyroid activity and the blood amylase.<sup>2</sup> These observations have been extended on more than one hundred patients. Feeding of thyroid substance to hypothyroid individuals lowers the blood amylase; it falls by as much as 50 per cent where thyroid medication is pushed to the point of toxicity. In untreated patients with thyrotoxicosis values, far below normal limits are common; clinical improvement after treatment and operation is accompanied by rise in blood amylase. The latter may lag considerably behind the other phenomena associated with restoration to normal thyroid status; indeed, some patients have developed postoperative myxedema at a time when the amylase has risen only to the lowest limits of normal range.

The behavior of blood amylase in the immediate postoperative phase is no less interesting. Serial observations show a large fall, usually within eight hours of thyroidectomy for toxic goiter; the low level is maintained for forty-eight hours, followed by a slow rise which may not have reached the preoperative level by the time the patient is discharged from the hospital. On the contrary, the enucleation of a nontoxic, solitary adenoma from an otherwise normal thyroid gland is not followed by alteration of the blood amylase.

This investigation was started in 1934 and the results as outlined above seem convincing to us as a conclusive indication of impaired liver function in thyrotoxicosis. While the assumption would be that all functions of the liver would be impaired, though not necessarily equally,

Minot (quoted by Jordan, 1930, pp. 192-193), regard the original angioblast, very early differentiated from mesenchyme, as the sole future source of endothelium, to which is ascribed a strict specificity throughout development. The advocates of the *in situ* method of origin, Huntington (1911, pp. 272-274), Miller (1912, pp. 489-490), Maximow and Schulte (quoted by Jordan, 1930, p. 193), on the contrary, conceive early vasculogenesis as a process of progressive fusion of tissue spaces and mesenchymal cells involving a continued differentiation of endothelium from mesenchyme.

*The Angioblast Theory.*—McClure (1921, p. 220) states that it has been observed in meroblastic ova, like those of the domestic fowl, that blood vessels and blood cells seem to make their first appearance on the yolk sac and then appear at a somewhat later stage of development in the body axis of the embryo. The early appearance of the blood vessels on the yolk sac led His (quoted by McClure, 1921, p. 220) to infer that certain cells on the yolk sac, which have been described by some as derivatives of entoderm and by others as derivatives of mesoderm, undergo an early differentiation to form a specialized tissue from which the endothelium of the yolk sac vessels and blood cells are exclusively derived.

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# Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

## CONGENITAL ARTERIOVENOUS ANASTOMOSES\*

STANLEY J. SEEGER, M.D., MILWAUKEE, WIS.

### I. INTRODUCTORY STATEMENT

**A**BNORMAL arteriovenous anastomoses are usually classified as congenital or acquired. The pathologic varieties are not to be confused with the normal communications between arteries and veins by means of which arterial blood passes from an artery to a vein without passing through a capillary bed. The existence of these latter "derivating channels" in nature has been recognized for many years. The former, or pathologic, varieties, recognized clinically because of the production of various signs and symptoms, while they are arteriovenous anastomoses, should more properly be referred to as arteriovenous fistulas. The so-called normal varieties are usually referred to as arteriovenous anastomoses. In this thesis arteriovenous fistulas will be characterized as AVF's, while arteriovenous anastomoses of the supposedly normal type will be referred to as AVA's.

The subject is one of many ramifications. This thesis is confined to a discussion of several of the relevant problems as follows: the historical background of arteriovenous anastomoses with a study of our knowledge of the genesis of the blood vessels; the anatomy, physiology, and pathology of arteriovenous anastomoses; a discussion of materials and methods used in studying blood vessels at Marquette University; and personal observations on laboratory material and clinical cases.

### II. HISTORICAL BACKGROUND OF ARTERIOVENOUS ANASTOMOSES

*A. Genesis of the Blood Vessels.*—Since endothelium is the essential tissue of the vascular system, the question has naturally arisen as to the manner in which this endothelium makes its appearance in the course of ontogeny; also, where and when it arises in the embryo and how the endothelial-lined channels of the vascular system are established. According to McClure (1921, p. 219), two opposing theories have been advanced by European anatomists in answer to these questions: The angioblast theory of His, and the local origin theory. The advocates of vasculogenesis by invasion, Evans (1909, pp. 315-317), Bremer (1914, p. 464), and

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endothelium invariably arises from some preexisting endothelium. If it did not arise in this manner, it would have a local origin from some tissue other than endothelium.

The implied specificity of yolk sac angioblast, the origin from it of intraembryonic endothelium by a process of continuous growth, and the necessity thereby implied that all intraembryonic endothelium arises from some preexisting endothelium constitute the logical claims of the adherents of the angioblast theory.

*The Local Origin Theory.*—The view opposed to the angioblast theory is that of local origin. According to this view, mesenchyme may become vascular tissue in almost every region of the body. The cells which bound an intraembryonic blood vessel are not in direct lineage with those which line the early vessels on the yolk sac. They have not come into being as an ingrowth from the early yolk sac vessels or angioblast, and they have not necessarily come from preexisting endothelial cells, although some of them may have had such an origin, inasmuch as local origin does not preclude the possibility of growth during or following the process of local vascular formation. Addition to endothelium may take place (1) by proliferation of endothelial cells already formed; (2) by addition of single mesenchyme cells; (3) by addition of solid cell aggregates; (4) by addition of already formed endothelial cavities, the lining of cells of which have differentiated locally, in and from the mesenchyme; and (5) by the active migration and alignment of single mesenchyme cells to form vascular cavities. The local origin theory holds that blood cells are not necessarily descended from a primitive yolk sac angioblast, but that mesenchyme within the embryonic body is capable of giving rise to blood cells. Advocates of the local origin theory do not believe that the vascular anlage is necessarily differentiated at a very early stage of development, as claimed by His (quoted by McClure, 1921, p. 222),\* or collectively and at one time, as stated by Minot (quoted by McClure, 1921, p. 222). Advocates of the mesenchymal theory recognize that there are certain regions in which a precocious production of vascular tissues takes place, but they claim that such regions are not the only regions in which such tissues are formed. Advocates of the local origin theory recognize various intraembryonic regions in which there is a first-hand production of vascular tissues, even relatively late in ontogeny, quite independent of such processes in the yolk sac. The angioblast theory regards endothelium as a tissue of high specialization quite foreign in nature to mesenchyme and quite removed from it genetically. The local origin theory claims that mesenchyme can transform into endothelium and that endothelium can change to mesenchyme.

McClure (1921, p. 223), in discussing the work of Florence Sabin on the development of the lymphatic system, states that in her early work

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she believed that her results confirmed the angioblast or ingrowth theory of His. Viewed in this light, the endothelium of the lymphatics, like that of the blood vessels, would possess a marked specificity. It also could be traced back directly and continuously to a unit vascular anlage known as the angioblast. One theory favored by Sabin (1917, pp. 118-120) is that there is a limited period for the differentiation and growth of angioblasts out of undifferentiated mesenchyme and that after this period all new blood vessels arise from the growth or proliferation of older angioblasts. Another theory advanced by her is that angioblasts continue to differentiate out of mesenchyme indefinitely. If the former is correct, the problem is to determine which differentiate and which are formed from preceding vessels. McClure (1921, p. 232) reviews the history of research in this line. He discusses the papers of W. C. Clarke, Miller (1912, pp. 489-490), and McWhorter and Whipple (1912, pp. 121-127). Clarke (quoted by McClure, 1921, p. 232) showed that vascular endothelium, wherever encountered, hemal or lymphatic, may be an instance of the environmental adaptation of an originally isodiametric mesenchymal cell subjected to mechanical influence. From his analyses of the results of various investigations, McClure (1921 p. 235) believes that it is evident that the morphologic evidence favoring the general principle of a local origin of intraembryonic endothelium from mesenchyme has been completely confirmed by experiment, and accordingly that the angioblast theory, in the sense maintained by His, therefore, no longer holds. He believes that while differences of opinion may still exist, as regards details of the process, both for the lymphatic and blood vascular systems, it is plain that the general principle of the local genesis of intraembryonic endothelium from mesenchyme may now be regarded as an established fact.

Jordan (1930, p. 192) holds that the total evidence seems to favor the view that in earliest stages blood vessels may arise in the mesenchyme of the embryo and that these primitive stems may be added to by discrete anlagen all of which may fuse to form the vascular net out of which develop the future main vessels. The vessels of later embryonic and fetal stages probably arise solely as sprouts from these earlier stems. He believes that the chief point of uncertainty concerns the point in time when vasculogenesis passes from a process including sprouting and fusion of separate anlagen to one when extension occurs exclusively by terminal growth. Both arteries and veins have a like origin in capillary plexuses. The final anastomosing sprouts of endothelium represent the definitive capillaries. The development of the definitive wall of arteries and veins involves the formation of extraendothelial layers of muscular and connective tissue elements from the surrounding mesenchyme and also their association into the several tunics of the various subdivisions of these vessels.

Swindle (1935, pp. 7-9), in discussing his observations relative to the formation of arteriovenous connecting channels, states that as an em-



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laries vary from  $\frac{1}{3,000}$  to  $\frac{1}{2,000}$  of an inch in diameter and from  $\frac{1}{20}$  to  $\frac{1}{30}$  of an inch in length, while Cunningham (1931, p. 872) states that the average diameter of the capillaries varies from  $8\mu$  to  $12.5\mu$  and that the average length is 0.75 mm. Krogh (1929, p. 24) states that the capillaries have practically never been counted, and means are wanting in the reports of much of the work which has been done to ascertain the size of the structures which have been graphically depicted. In most tissues the arrangement of the capillaries is so complicated that the difficulties in the way of even approximate measurements are very formidable. The capillaries in a given field often vary considerably in diameter. They sometimes may be so narrow that they cannot admit red corpuscles even when these are greatly compressed. On the other hand, in the human skin the diameter may be as large as 0.02 mm. (Krogh, 1929, p. 34). Mall (quoted by Krogh, 1929) describes the average diameter of the capillaries in the intestinal villi as  $8\mu$  to  $5\mu$ . On other areas of the intestine they are of about the same diameter, and from 0.4 to 0.2 mm. in length. In injected specimens of the intestinal villi, Krogh (1929, p. 40) found them to be of an average diameter of  $12\mu$ . Vimtrup (quoted by Krogh, 1929) states that the average diameter of capillaries in the kidney glomeruli is  $10\mu$  and the average length is 0.5 mm.

Krogh (1929, p. 29) gives the number of capillaries per square millimeter as  $1,350 \pm 31$  in the gastrocnemius of the horse. The transverse section of an ordinary pin is 0.5 mm. It requires some mental effort to conceive how there can be room within such a pin for about 700 parallel tubes carrying blood, in addition to about 200 muscle fibers. In other animals he states that the number of capillaries per millimeter may be even greater. There seems to be some relation between the number of capillaries and the metabolic activity. In the dog's semimembranosus muscle there are  $2,630 \pm 51$  per square millimeter. In the smallest mammals there may be as many as 4,000 per square millimeter. In cold-blooded animals, such as the cod and frog, there may be about 400 per square millimeter. Krogh (1929, p. 29) states that there should be a study of the quantitative anatomy of muscle capillaries.

In human skin, according to Krogh (1929, p. 34), on the dorsum of the hand there are 64 capillaries per square millimeter. In the forearm, 47; cheek, 16; and in the circumoral skin, 20. It is a characteristic feature of the blood vessels of the human skin that there is no very sharp distinction between the smallest arterioles ("capillary arteries"), the capillaries proper, and the venules ("capillary veins"). The venules in the outer part of the cutis are so thin walled and present such a large total surface that they have practically taken over the normal function of capillaries.

Capillaries in the rete mirabile annexed to the oxygen gland in the eel are 4 mm. long (Krogh, 1929, p. 34). The organ is 8 sq. mm. across.

bryonic AVA grows in length, it loops away from its original position and divides into two or more parts wherever the surrounding tissue causes opposite walls of the anastomosis to come in contact with one another. Some observations made principally on viviparous snakes show that at the point of contact of the opposite walls these walls fuse to form two or more blood channels out of one and that the newly created vessels may separate widely from one another. Each of the new vessels may loop away in different directions and divide into two or more parts, and so on until the original anastomosis consists of a principal arterial trunk and a principal venous trunk which lie side by side and which are connected with one another at numerous points by relatively small arterial and venous branches and capillary networks. This metamorphosis may be of such a nature that the original AVA finally consists essentially of an arterial network, a venous network, numerous arteriocapillary anastomoses or terminal arterioles, numerous venocapillary anastomoses or terminal venules, and numerous capillaries.

In some tissues of the body, as in or near the cartilage of the pinna, some of the embryonic AVA's cannot loop away from their original positions. They are held in place by the solid tissues about them. These accordingly persist as relatively simple arteriovenous connections instead of very complex ones. Under certain conditions of congenital, partial obstruction of the flow of venous blood in a vein, embryonic AVA's fail to undergo metamorphosis at points somewhat centrally to the points of obstruction. Embryonic AVA's may accordingly persist in a tissue in which they are not ordinarily found. For instance, two persisting AVA's were found in the wall of the stomach of a human fetus, situated centrally to the point at which an artery is choking the vein. The metamorphosis of an AVA into an arterial and a venous trunk and their branches implies growth. It is important to observe in this connection that the growth and the resulting metamorphosis of the AVA's fail to occur at points where there is relatively little venous blood in the vein (due to venous obstruction) and a relatively large amount of arterial blood in this vessel (due to the inflow through the AVA or AVA's from the artery). Swindle (personal communication) has made the interesting observation that in the hearts of the Bovidae and Cervidae arterial anastomoses, connecting the longer arteries, are present. These disappear during development to the adult form, and the remaining arteries are then end arteries in the sense of Cohnheim.

B. *The Anatomy of the Capillaries.*—It is generally accepted that the normal means of communication between arteries and veins is through a capillary bed. In studying AVA's, which may be considered either as abnormal structures or as representing an arrangement which is different from that usually considered as normal, it is well to review briefly our knowledge of the capillary bed. The anatomic literature is disappointing in its report of the number, distribution, and surface of the capillaries. Gray's *Anatomy* (1907, p. 584) merely states that the capil-

present in about equal numbers. At best, one observes occasional cases in which no conclusion can be drawn relative to capillary morphology. In Brown's studies the average total length of the visible capillary loop in the normal group was 0.42 mm. The average caliber of the arterial limb was 0.007 mm.; and of the venous limb, 0.009 mm. These are the averages of a group of 110 approximately normal persons from the ages of twenty to ninety-five years. The normality of these persons was based on the absence of demonstrable disease and normal cardiorenal vascular findings for their age.

Cowdry (1934, p. 102) comments on the fact that the capillaries may not only be absent and their place taken by AVA's, but it is also possible that contrary to the general rule, they may not form a closed system of vessels in the spleen. Kyes (1901, pp. 37-43) stresses "the lack of demonstrable continuity of vascular connection between the ultimate capillaries of the arterial and venous systems." It remains to be discovered whether in this locality the endothelial walls are continuous or whether they exhibit openings which allow the blood cells to escape into the surrounding tissue. Maximow and Bloom (1930, pp. 399-400) claim that the transitional vessels are not lined with endothelium but by expanded reticular tissue, and that the manner in which blood passes from arterial capillaries into venous sinuses is not known. If this contention is proved to be correct, this is the second locality in which the blood stream is not limited by the walls of endothelium, the first being the circulating maternal blood in the placenta which is confined to spaces lined with tissue of ectodermal origin.

*C. The Anatomy, Physiology, and Pathology of Arteriovenous Anastomoses.—*

*Anatomy.*—According to Krogh (1929, p. 100), in the anatomic literature of fifty years ago there are a number of references to the existence of "derivating channels," represented by small arteries opening directly into somewhat larger veins. Much of this early evidence for the presence of such direct connections was based upon the appearance in the vein of suspension of granules, injected into arteries, the consistence of which was presumably too large to enter capillaries. With the work of Hoyer (quoted by Krogh, 1929, pp. 100-106), the presence of AVA's in various regions of different animals was demonstrated conclusively by a number of different staining and injection methods. Hoyer found such anastomoses in the ear of the rabbit, cat, and dog, and in the tip of the nose, in the lips, toes, the tip of the tail, and the cavernous tissue of the sexual organs of most mammals. In man he was able to demonstrate them only in the hand and foot (especially in the fingers and toes) and in the sexual organs. Histologically, Hoyer described connections from artery to vein as pursuing a straight course, or, more frequently, a winding one. Their wall he found to be thick and muscular on the arterial side and thin walled at the funnel-shaped venous portion. Hoyer (quoted by

The capillary surface is venous, 106 sq. mm.; arterial, 105 sq. mm. The volume of the capillaries is venous, 25 c.c.; and arterial, 18 c.c. The desirability of extending our knowledge of the anatomy of the capillaries is obvious, and Krogh, in his excellent monograph on the *Anatomy and Physiology of the Capillaries*, makes a plea for their study from the standpoint of quantitative anatomy.

Brown (1925, p. 57), of the Mayo Clinic, states that in studying the form and behavior of capillaries it is exceedingly difficult, in certain instances, to determine where the normal leaves off and the pathologic begins. In many apparently normal persons occasional loops are short and tortuous, dilated or contracted, or are otherwise abnormal. The granular appearance of the flow or the cessation of flow, and plasma gaps may also be observed in single loops. Brown thinks that in the normal person, however, these are isolated phenomena. Not until the majority of the loops are abnormal in form and flow are the capillaries classified as pathologic. When a sufficient number of capillaries reveal stasis with dilatation, a definitely recognized cyanosis will exist; and when a sufficient number are empty or only partially filled, pallor of the skin will be recognized macroscopically. Ebbecke (quoted by Brown, 1925) has shown that the degree of dilatation of the capillaries and venules determines the color of the skin, while arterial dilatation determines the heat of the skin. In differentiating the pathologic from the normal, the quantitative changes, rather than the qualitative, indicate disease. Abnormal capillaries, in the absence of clinical manifestations, occasionally are encountered.

That the capillaries have an independent contractility seems reasonable. These vessels exhibit responses perhaps more delicate than those of the larger vessels. This would be expected on the basis of structure and function. According to Krogh (1929), anatomic researches have demonstrated contractile or Rouget cells with fine fibrillae wrapped about the endothelial tube. The transitional point from arteriole to capillary, or from capillary to venule, is not always well defined in the vessels of the skin. In lower orders and certain capillaries of mammals the transitional point is definite.

The studies of Brown (1925, pp. 59-62), of the Mayo Clinic, have shown that the capillary undergoes involutionary changes with advancing age, probably similar to those observed in the larger vessels. The capillary apparently becomes longer; the calibers are narrowed; and the increased length may manifest itself as a long, straight, or tortuous loop. According to Brown, the usual normal type in the young adult is the hairpin shape, fairly regular and uniform, but there are variations. Occasionally young persons have uniformly thick, tortuous loops. The absence of narrowed lumina seems to differentiate these from the pathologic tortuous types. The greatest difficulty in distinguishing diseased capillaries arises in cases in which the normal and abnormal types are

Krogh concludes that it follows from the observations of Heimberger that his "derivating channels" which are distal to those of Hoyer and Grosser must be able to contract and expand and to close up entirely.

Grant (1930, pp. 282-283) found anastomoses in all parts of the rabbit's ear. He states that they are most numerous on the dorsal surface of the thinner portion and are situated in the deeper layer of the skin and on the surface of the underlying perichondrium. On three portions of perichondrium from the dorsal aspect of the ears of three rabbits, two portions measuring 13 by 8 mm., and one, 12 by 9 mm., no less than 65, 53, and 46 separate communicating channels were counted by him; that is to say, about 1 to 1 or 2 sq. mm. in the average. They are mostly tortuous vessels, arranged in groups, uniting neighboring arteries and veins. Less commonly they form short lateral communications between parallel vessels or an artery may approach a vein and open directly into it. They vary in size, the internal diameter of the arterial side measured in optical section being from 20 to 70 $\mu$ . This agrees with the diameter of the column of blood flowing through them when maximally dilated during life. The arterial is narrower than the venous end, the difference being slight when the vessel is dilated; when the arterial side is constricted, the channel is funnel shaped. Grant (1930, p. 283) states that structurally the anastomoses fall into three sections. On the arterial and on the venous sides they have the usual structure of these vessels, though the wall of the arterial portion is thicker than in arteries of a corresponding lumen, the adventitia being stouter and the muscle cells more numerous. The third section, the region of transition, Grant states, is not so simple as Hoyer depicts it; it is more accurately represented by Grosser's description of anastomoses in human skin. In this region the adventitial and muscular thickening is greatest; the muscle nuclei are shorter and rounder and are not arranged so regularly around the vessel. The numerous nuclei in the sphincter-like thickening give the anastomoses a dark color rendering them conspicuous. The adventitial thickening is continued, decreasing for a short distance on the expanding venous end though the muscle cells cease or become sparse rather abruptly.

Clark and Clark (1934, p. 281) viewed living AVA's in the rabbit's ear through special chambers introduced by operation. They found that AVA's were visible in all chambers immediately after the operation. In stable chambers they numbered from 25 to 55 in the observation area of 1.6 sq. cm., being more numerous in rabbits with an active circulation. Followed over a period of months, they were found to be relatively permanent structures, fully as persistent as arterioles and far more so than venules and capillaries.

According to these workers, the arrangement of AVA's was found to be varied. The majority arose from smaller arteries, but a certain number arose from larger arteries; others, from arterioles; others formed the

Krogh, 1929, pp. 100-106) made a search for these "derivating channels" in many other places, but, apart from the case of the arteries opening directly into the corpora cavernosa, he found them only in such projecting parts as might require a considerable supply of blood to keep them warm when exposed to low temperatures.

Following Hoyer, several other investigators have studied AVA's histologically. Among these Krogh (1929, pp. 100-106) mentions especially Grosser, who confirmed Hoyer's results and who gave excellent descriptions of the finer structure of such direct connections in the toes of various mammals, including man. Grosser found them to be numerous in the skin of human fingers where they are arranged in small groups, 1 to 2 mm. apart. Their musculature is twice to thrice as strong as that of arteries of the same bore (about 0.02 mm.), and they are imbedded in connective tissue with numerous nuclei. They are common, also, within the digital bones where they are surrounded by a venous plexus which allows them to open and close freely. They are especially large (0.1 to 0.2 mm.) in the thumb of bats. Grosser has made a search for them in appropriate places in reptiles where they appear to be absent. Swindle (personal communication) stated that in numerous injections in bats he has been unable to confirm the presence of AVA's in this animal.

In the last few years evidence has been brought forward for the existence of AVA's from intravital observations of the circulation in the human skin. Heimberger (quoted by Krogh, 1929, p. 102) has been able to observe such connections directly and in considerable numbers in the fingers of persons having a very delicate skin. He describes them as short connections between peripheral arterioles and venules, short circuiting the long capillary loops. He finds these channels, normally closed, to be opened up for a short period by weak mechanical stimulation. Krogh states that he should not attach much weight to these observations, which must be exceedingly difficult to verify, but for the two facts that Heimberger is an observer of quite extraordinary ability and patience, and that his direct findings are supported by observations of the blood flow in superficial venules and capillaries which are explicable only if AVA's exist in close proximity to the vessels under observation. In a few cases Heimberger reported seeing pulsation of the blood in venules when the corresponding arterioles were closed and the blood in the capillaries quiescent. As Krogh points out, this is possible only when the venule in question possesses another connection with the arterial system, through which the pulse is admitted. In other cases the blood is seen for some time to flow back from a venule through the capillaries to an arteriole, which postulates that the venule is connected directly with a somewhat larger artery, transmitting sufficient pressure to carry the blood back into an arteriole which must also be in direct communication with a larger vein.

TABLE I  
NUMBER OF ANASTOMOSES PER 1 CM. SURFACE AREA

Hand	
Index finger	
Nail bed	501
Tip	236
Palm, 3rd phalanx	150
Palm, 2nd phalanx	20
Palm, 1st phalanx	93
Palm	
Metacarpophalangeal joint. 3rd finger	31
Thenar eminence	113
Hypothenar eminence	96
Foot	
2nd toe	
Nail bed	593
Pad	293
So'e—near heel	197

numerous rounded nuclei. In appearance they are not unlike the ducts of the sweat glands. They found the anastomoses to be arranged chiefly in groups situated at the level of, or a little superficial to, the sweat glands. They are thus much too deeply placed to be seen from the skin surface during life. They are mostly tortuous channels and open into a rich network of thin-walled veins. Their lumina in their preparations varied from 20 to 70 $\mu$ , the average being 35 $\mu$ . Grant noted that the diameter of the anastomoses in preparations of the rabbit's ear made by this method agreed well with their diameters measured when maximally dilated during life. Grant and Bland (1931, p. 393) also injected a full-term stillborn fetus, but they found no anastomoses in places where they found them in adult skin. In this connection they noted that Grosser and others failed to find anastomoses in newborn or fetal material.

Krogh (1929, p. 106) states that in a very recent publication Wearn (1928) demonstrates the existence of anastomoses in the heart of man and other mammals between the coronary artery and the Thebesian veins. These latter vessels normally drain off a considerable portion of the venous blood from the heart muscles directly into the right and left ventricles. The anastomoses with the artery are opened up when the heart, which has ceased beating, is dilated by injection. Their function during normal life is entirely unknown, but Wearn mentions two human cases where it was found at autopsy that the orifice of the coronary artery was entirely occluded and that the heart muscle could receive its blood supply only through these anastomoses. The occlusion had developed slowly but was of long standing, and the supply through the Thebesian anastomoses had enabled the patients to lead a normal working life.

A peculiar anomaly, an arteriovenous communication between the right coronary artery and the coronary sinus with aneurysmal dilatation of the parts involved, is described by Halpert (1930). The condi-



termination of an artery; and clusters of three or more from the same artery were frequently seen. The veins into which a number of AVA's emptied were usually large, while occasionally they had a fairly thick muscular wall and showed definite contractility.

Clark and Clark (1934, p. 282) state that the two forms of AVA's described by Hoyer, straight and coiled, were seen by them in the living preparations. In studies extending over weeks or months, the lengthening of certain AVA's, due to stretching, and the bending of others, apparently due to slight compression, were observed. The division into three parts, the arterial, the narrow thick-walled intermediary portion, and the thin-walled, funnel-shaped venous portion, was also seen in the living AVA's and, as a rule, the intermediary portion showed the most active contractions, while the funnel did not contract. Although typical, this form is not the only one, however, as AVA's were observed in which the muscular wall extended from artery to vein with little differentiation in form or contractility. Variations in size (diameter or lumen) of living AVA's were marked in different AVA's in the same area and in the same one on different days, while the diameter of a single AVA frequently changed several times per minute, according to the degree of dilatation or contraction.

From their studies, Clark and Clark (1934, p. 239) found that anastomoses, in addition to being normally present in large numbers in the rabbit's ear, are relatively permanent. That new anastomoses occasionally formed in the chamber areas seemed certain, although here again care was necessary in order to be sure that a supposedly new anastomosis was not merely a preformed one which had remained closed for some time and then reopened. In several chambers, however, the appearance of a new anastomosis was observed in a region which had been submitted to extensive study, part of the time with higher microscopic magnification, for months. Despite the formation of occasional new ones, the apparent loss of a few others and the undoubted changes of formation of many individual anastomoses observed, a cross-connection between a given artery and vein once located could be identified, in the majority of cases, at the same site over a period of months. Anastomoses appeared to be fully as stable in form and position as the smaller arteries and larger veins, and conspicuously more so than the venules and capillaries which have been shown to be remarkably labile.

Their observations on the distribution of anastomoses in the human skin are summarized in the following table by Grant and Bland (1931, p. 393). Anastomoses are absent from dorsum of fingers, toes, hand, and foot; from flexor surface of lower forearm and lower calf of leg, and from lower half of ear.

The authors Grant and Bland (1931, p. 392) state that the anastomoses are especially conspicuous by reason of their thick walls with

vascular reaction but are the vessels chiefly responsible for the increased blood flow. Grant and Bland (1931) point out that the presence of anastomoses in the skin is not essential to the development of the temperature reaction; for example, although they are apparently absent from the lobe of the human ear, yet the lobe usually reacts vigorously when cooled. They think it may be that the hand and foot, exposed at the end of long limbs and often in contact with cold surfaces, require a special vascular arrangement, which is not needed in the ear, adequately to protect them against cold; or it may be that the anastomoses in the hand and foot, while playing an important part in the reaction to cold, are restricted chiefly to these regions for some special and unknown reason. From their limited distribution, it seems to these authors that they are little more than a minor factor in the regulation of body temperature in man in whose relatively hairless body other mechanisms are more effective for this purpose. That they serve different functions in different parts of the body seems to them likely. Of some of their functions there is evidence, namely, maintenance of the temperature of exposed parts and regulation of loss of heat. It has been suggested, first by Muller (quoted by Grant and Bland, 1931), that anastomoses are responsible, at least in part, for erection of the penis. Of other functions we are as yet ignorant and even speculation fails to suggest a purpose for the AVA's in the human glomus coccygeum. Grant and Bland note the anatomic relationship between AVA's and Pacinian corpuscles which they state were described by Grosser and Schumacher. They emphasize that the activity of AVA's under various conditions, such as have been described, and their presence in large numbers in certain parts of the animal body, should be borne in mind in a variety of circumstances. For example, they introduce a disturbing element into the interpretation of changes in capillary pressure measured at the base of the finger nail and because of their presence, pressure changes observed here during hyperemia cannot be taken as representing those occurring in other regions where anastomoses are wanting. Again, their ready response to various stimuli should not be neglected in experiments on the blood flow through the limbs of cats and dogs, especially in relation to the action of drugs. Further, since they have been described by previous workers as present in a number of animals, not only in the ears, nose, and feet, but also, among other places, in the pia mater of the brain, in the capsule and parenchyma of kidney, and in the corpus cavernosum of the penis, the authors believe, that they must be taken into account in dealing with the circulation in these and other parts of the body. In this connection, however, Grant and Bland (1931) believe it is to be emphasized that many of the older statements as to the presence or absence of anastomoses throughout the body require confirmation. Thus, for example, while they found numerous and large communications between the arteries and veins on the perichondrium at the

tion was an incidental finding at necropsy in a patient, adult man (aged fifty-four years), who died of carcinoma of the stomach and who presented during life no clinical evidence suggesting a cardiac defect.

Grossly abnormal arteriovenous communications have been recognized for many years. Reid (1925, b, p. 996) states that both Antyllus and Albucasis accurately noted the physical signs of a condition we now recognize as arteriovenous aneurysm, although they did not recognize its cause and, therefore, could not give to it the name of arteriovenous aneurysm. According to Reid, the condition of abnormal arteriovenous communications was first accurately described by William Hunter in 1757. Callander, in 1920, collected 447 cases of all kinds, 3 being congenital. Reid, in 1925 (1925, a), reported 33 cases of abnormal arteriovenous communications. Twenty-seven were acquired and 6 congenital. Lewis, in 1930, collected 33 cases in the literature (congenital). These include the cases of Reid and 3 from the Mayo Clinic. Horton, in 1931, reported 24 cases from the Mayo Clinic between the years 1929 and 1931, and in 1934 he reported 38 cases seen up to that time. In only one case was the diagnosis made before entrance to the Clinic. In 19 cases reported by Lewis, surgical exploration was carried out. This was followed by amputation in 11 cases, and surgical cure was obtained in only 1 case. The report of 1 case is here added.

*Physiology.*—Grant (1930, p. 281), from his observations on direct communications between arteries and veins in the rabbit's ear, concludes that we have no conception of the function of AVA's based on experiments. Flushing of the ears is dependent on the temperature to which a rabbit's body is exposed, rather than that to which the ear is exposed. He (Grant, 1930, pp. 283-300), found that the anastomoses in the rabbit's ear react to mechanical stimulation, histamine, acetylcholine and cold, by dilatation, and to adrenaline by contraction. They can be dilated by the local axone reflex, and they are particularly responsive to sympathetic impulses, contracting vigorously. Stimulation of the sympathetic with faradic current, he found, causes contraction. An unusually rich distribution of the perivascular nerve plexus to the AVA's is described. The anastomoses, according to Grant (1930), serve two functions: (1) local—it is mainly through their agency that the temperature of the ears is maintained when these are exposed to cold; (2) general; they are important factors in regulating body temperature, aiding in the dispersal of heat by allowing an enormous blood flow through the ears. Grant and Bland (1931) confirm these observations. They found numerous anastomoses present in the bird's foot and found that the foot responds to cooling by a vigorous temperature reaction. In man many anastomoses are found in the palm of the hand and sole of the foot and they are particularly numerous at the ends of the digits. These parts also react strongly when cooled, and they state there are reasons for believing that the anastomoses not only take part in the

vascular reaction but are the vessels chiefly responsible for the increased blood flow. Grant and Bland (1931) point out that the presence of anastomoses in the skin is not essential to the development of the temperature reaction; for example, although they are apparently absent from the lobe of the human ear, yet the lobe usually reacts vigorously when cooled. They think it may be that the hand and foot, exposed at the end of long limbs and often in contact with cold surfaces, require a special vascular arrangement, which is not needed in the ear, adequately to protect them against cold; or it may be that the anastomoses in the hand and foot, while playing an important part in the reaction to cold, are restricted chiefly to these regions for some special and unknown reason. From their limited distribution, it seems to these authors that they are little more than a minor factor in the regulation of body temperature in man in whose relatively hairless body other mechanisms are more effective for this purpose. That they serve different functions in different parts of the body seems to them likely. Of some of their functions there is evidence, namely, maintenance of the temperature of exposed parts and regulation of loss of heat. It has been suggested, first by Muller (quoted by Grant and Bland, 1931), that anastomoses are responsible, at least in part, for erection of the penis. Of other functions we are as yet ignorant and even speculation fails to suggest a purpose for the AVA's in the human glomus coccygeum. Grant and Bland note the anatomic relationship between AVA's and Pacinian corpuscles which they state were described by Grosser and Schumacher. They emphasize that the activity of AVA's under various conditions, such as have been described, and their presence in large numbers in certain parts of the animal body, should be borne in mind in a variety of circumstances. For example, they introduce a disturbing element into the interpretation of changes in capillary pressure measured at the base of the finger nail and because of their presence, pressure changes observed here during hyperemia cannot be taken as representing those occurring in other regions where anastomoses are wanting. Again, their ready response to various stimuli should not be neglected in experiments on the blood flow through the limbs of cats and dogs, especially in relation to the action of drugs. Further, since they have been described by previous workers as present in a number of animals, not only in the ears, nose, and feet, but also, among other places, in the pia mater of the brain, in the capsule and parenchyma of kidney, and in the corpus cavernosum of the penis, the authors believe, that they must be taken into account in dealing with the circulation in these and other parts of the body. In this connection, however, Grant and Bland (1931) believe it is to be emphasized that many of the older statements as to the presence or absence of anastomoses throughout the body require confirmation. Thus, for example, while they found numerous and large communications between the arteries and veins on the perichondrium at the

tip of the rabbit's ear, they failed to discover in two rabbit and two dog kidneys and one human kidney anastomoses such as, they stated, have been described by Geberg and Golubew. It seems clear that many more anatomic and physiologic data require to be collected on these interesting direct communications between arteries and veins.

Grant and Bland (1931, p. 306) summarize their conclusions as follows:

1. Numerous AVA's are present in the foot of the domestic hen and duck.

2. The foot of these birds responds to cooling by a vigorous temperature reaction closely resembling that of the human finger.

3. In man many anastomoses are present in the sole of the foot and palm of the hand and they are particularly numerous at the ends of the digits.

4. These are the parts that also react strongly to cold, the reaction being best displayed where anastomoses are most numerous.

5. Though other parts of the body yield a temperature reaction in the absence of AVA's, the authors believe that in the extremities the anastomoses not only take part in this vascular reaction but are chiefly responsible for the increased blood flow.

6. Because of their activity under various conditions and their presence in large numbers in certain parts of the animal body, AVA's require to be taken into account in dealing with the peripheral circulation.

Clark and Clark (1934, pp. 282-284), in their studies of living AVA's in the rabbit's ear, found that those AVA's most exposed during the operation remained dilated and noncontractile for hours or days, while the deeper ones, like the arterioles, usually remained narrow or closed. Subsequently, the dilated AVA's narrowed or closed completely for a period, while the others widened. Spontaneous periodic contractions of most of the AVA's in the chamber returned within two days to a week after the operation, although an injured AVA or portion thereof might remain dilated and paralyzed for a longer period. The difference in recovery rates was probably due to varying degrees of nerve injury.

AVA's in stable chambers were seen by Clark and Clark (1934) to contract and dilate spontaneously, each at a rhythm which was usually independent of that of the artery from which it arose or from that of other AVA's in its immediate vicinity. The behavior of individual AVA's frequently varied from day to day, even with surrounding conditions as nearly uniform as possible. The active opening and closing of AVA's had a marked effect on the direction, speed, and volume of blood flow in the veins into which they emptied.

Mild stimulation (tactile) of the rabbits caused the AVA's to contract with the arteries. Sudden noises also caused contraction of the AVA's with the arteries, although an exception on the part of one AVA was noticed on one occasion. In sleep, with arteries all dilated and

sluggish circulation, many of the AVA's also widened, while others contracted tightly, and still others continued to open and close rhythmically.

Clark and Clark (1934, p. 283) state that, in general, AVA's, like arteries, were wider at warmer and narrower at cooler temperatures, although with moderate changes in either direction the contraction rhythm was maintained. Usually, local heating of the ear had to be as high as 40° C. before many AVA's ceased rhythmic contractions and remained dilated, although the arteries usually showed lengthening of the dilatation period at 32° C. to 36° C. However, some AVA's always continued to contract with no change in rate or length of the dilated period at temperatures of 40° C. to 44° C., while a few in each chamber failed to respond in any perceptible way to heating. Similar exceptions were noted with moderate degrees of cooling when most of the AVA's, like the arterioles, stayed narrow. An AVA which responded to heating or cooling in any one way on a certain day might behave quite differently on the next day. Within the moderate ranges of temperature used, a wide variety of individual reaction was always noted whenever a number of AVA's were kept under prolonged observation. AVA's located near regions of local infection, like the arteries, remained persistently wider than the normal vessels. In such cases the spontaneous contractions of the AVA's usually ceased before those of the neighboring arteries. However, Clark and Clark (1934, p. 284) observed an exceptional AVA, located near such an infected spot, which failed to widen and which continued to contract rhythmically. They found that stimulation caused contraction; while in sleep, some opened, some contracted.

In general, AVA's dilated with warmth and contracted with cold. The behavior to local heat and cold might vary from day to day. In areas of local infection they remain widely open.

In concluding their observations, Clark and Clark (1934, p. 281) state that perhaps the most striking characteristic of the living AVA's as shown by their study is their erratic behavior. General pictures of their usual activity can be given and general statements made concerning their reactions to change of temperature, to sleep, and to infection, but individual exceptions must be made in all of these cases. It would, therefore, seem inadvisable to base conclusions as to the behavior of AVA's in general upon observations of the reaction of a few of them on any one day.

Starling (1933, p. 1015), in discussing the physiology of AVA's, states that the blood flow through the skin is under the control of the central nervous system through the vasoconstrictor and vasodilator nerves, and when the skin is cooled it is by altering the size of the cutaneous vessels that the central nervous system chiefly acts in regulating heat loss. In cold weather or when heat production in the body is low, the vessels are constricted, the skin is cold, and the heat loss is small. In the extremities of the body, excessive skin cooling, with ensuing tissue damage, is

probably prevented by the opening up of the AVA's. In this way the skin surface is flushed with warm blood so that its cooling is delayed. The anastomoses are controlled, probably centrally, by constriction or dilatation of the arterioles.

*Pathology.*—In clinical medicine the existence of abnormal arteriovenous communications is recognizable by the presence of certain rather obvious symptoms and signs. The most common sites for the occurrence of AVF's are the head (scalp and intracranial), the neck, and the extremities. The relative rarity of these lesions in the trunk is of interest in view of Halpert's (1930) description of a congenital AVA in the heart and of Swindle's (1935, p. 3) finding of a congenital AVA in the walls of the fetal stomach. The changes produced by the presence of AVF's are usually grouped under the local, the regional, and the general or systemic. The local clinical picture as well as the nomenclature may be confusing. As Lewis (1930, p. 4) points out, it is frequently impossible to differentiate between various vascular lesions, for they may have several common characteristics. They are classified in diverse fashions by different authors. Reid (1925, b) believes that there is no essential difference between arteriovenous aneurysms, cirroid aneurysms (racemose aneurysms), arterial Ranken-angiomas or aneurysms by anastomosis, pulsating angiomas, and possibly simple angiomas. Reid believes that all are probably instances of abnormal arteriovenous communications, and, therefore, that the term arteriovenous aneurysm is all embracing. As he states, the medical profession has come to regard arteriovenous aneurysms as having to do with trunk line vessels and not with the very small arteries and veins. For instance, the condition that results when a blow on the head establishes a free communication between the vessels of the scalp is known as a cirroid aneurysm and not as an arteriovenous aneurysm. Matas (quoted by Reid) defined an arteriovenous aneurysm as any abnormal communication established between the arterial and venous channels. The terms hemangiectatic hypertrophy and congenital phlebarteriectasis have also been used to describe this condition.

According to Lewis (1930, p. 3), the arterial Rankenangioma (racemose or cirroid arterial aneurysm) has been defined as a vascular tumor in which all the arteries of a region, including their finest branches, often communicating with each other, are dilated and tortuous. Secondly, the veins, according to most authors, are involved. Wagner (quoted by Lewis, 1930) believes that the formation of new vessels is characteristic of an angioma of this type, that the newly formed vessels have a decided tendency to growth, and that there is an eccentric hypertrophy of the vessels of small caliber already existing. The arterial racemose aneurysm has been differentiated from lesions known as diffuse phlebarteriectasis and diffuse phlebeetasis. Diffuse phlebarteriectasis is supposed to be characterized by a progressive dilatation of an arterial bed

with its capillaries and veins, while in diffuse phlebectasis only the veins are involved in the dilatation. It would seem that the terms AVF and arteriovenous aneurysm are used rather indiscriminately. The fact that AVA's exist in what may be considered the normal state of many animals and the fact that clinicians recognize only the very obvious alterations produced by relatively large communications raise the question as to the existence of border line or unrecognizable AVA's. The term "arteriovenous fistula," in Horton's (1931) paper, is used to designate any abnormal communication or communications between arteries and veins by means of which arterial blood passes from an artery to a vein without passing through a capillary bed. It includes the various direct and indirect communications described in literature as cirroid aneurysm, arteriovenous aneurysm, pulsating venous aneurysm, arteriovenous varix, aneurysm by anastomosis, angioma cavernosum, angioma arteriale racemosum, aneurysm serpentina, and angioma arteriale.

Horton (1931, p. 665) states that he agrees with Dandy (1928, p. 192) that the various terms, "cavernosus," "racemose," "cirroid," and "serpentine," whether applied to arteries or veins, are merely descriptive of a superficial expression of a lesion and not of the fundamental pathologic process. The terms, he says, for the most part are useless and serve only to confuse the reader. The fundamental pathologic process is the same regardless of whether the arteriovenous fistula is in the foot or in the cranial cavity. Intracranial AVF's offer the best opportunity for a study of the gross appearance of the abnormal arteriovenous connections. Dandy (1928) observed that since the veins are free from all accessory coverings it is possible to see through the walls of the veins and detect the pulsing red arterial blood against a background of black venous blood. Cushing and Bailey (1928, p. 54), while exploring the great vessels of the neck in a well-advanced case of AVF (angioma arteriale), observed that the internal jugular vein was markedly enlarged and that "it looked much lighter in color than normal, and on inspection, though the vein was not definitely pulsating, one could see what appeared to be a current of arterial blood passing down in the venous stream." Horton (1931, p. 666) states that if one could only visualize the regional vessels and the abnormal arteriovenous communications in the extremities of the group of cases reported in his paper he believes that one would see the same pictures which have been so accurately described by Dandy and Cushing. He thinks this is amply indicated by the oxygen studies which were carried out. In each case there was a high admixture of arterial and venous blood in the regional or deep veins of the involved extremity. The bright red appearance of the blood in most cases was sufficient to warrant the diagnosis of an AVF.

Pemberton and Saint (1927, p. 791), in reviewing the effects of abnormal arteriovenous communications, describe the symptoms and signs. The usual effects may be considered from three aspects: the local, the



regional, and the general or systemic. The local effects, they state, are those manifested by the affected blood vessels. The blood from the artery flows into the distal part of the vein, greatly increasing the volume of blood in it and producing a pressure greater than the vein is normally capable of withstanding. As a result, the vein becomes dilated and tortuous. Similar changes take place, though probably not to such a great extent, in the proximal part of the vein. The larger the fistula and the longer its duration, the more widespread will be the venous involvement, in many cases almost all the veins of a limb which is the site of a fistula being affected. Reid (1920) found in experiments on dogs that there was an increase in the elastic tissue in the walls of an involved vein (the so-called arterialization). Pemberton and Saint (1927) were able to examine microscopically the veins in the vicinity of the anastomosis on one case only and found no evidence of arterialization, but calcareous degeneration was well marked in the internal part of the middle coat in one section.

The effect of an AVF on the involved artery, according to these authors, consists of dilatation, thinning of its walls, and degenerative changes in its coats, all of these changes taking place, in greater or less degree, only proximal to the fistula. Holman (1924, p. 816) has drawn attention to the fact that when the cross-section of the fistula is small these changes may be hardly noticeable or even entirely absent, although the fistula may have existed for many years; whereas, when the fistula is large, they are invariably present, particularly the dilatation and thinning, in marked degree. As to the cause of these changes in the proximal artery, opinions are somewhat divided. According to Pemberton and Saint (1927, p. 792), some authors believe that the diminished blood pressure causes loss of tone and functional inertia which results in the changes just described. The objection to this theory is that the diminished blood pressure is general and, since other arteries are not affected, it would seem that the cause is local rather than general. Others take the view that the increased amount of blood flowing through the artery is sufficient to account for them. Reid (1920, pp. 43-50) thinks that it would be unusual if a simple handling of an increased volume of blood by the proximal vessels did not lead to an hypertrophy and strengthening of their walls. While it is true that dilatation, thinning, and degeneration of the walls of the hollow viscera are often the sequelae of previous hypertrophy, yet this is not always so, and Pemberton and Saint (1927, p. 793) offer another explanation of these changes. In the first place, the dilatation is acute. In support of this are the observations that it is present only when the fistula is large and that it occurs almost at once after the production of the lesion. Second, the dilatation causes constriction of the vasa vasorum, and this results in diminished nutrition of the vessel wall, leading finally to thinning and degeneration.

The regional effects are those evident in the particular limb affected. The first is hypertrophy, as seen in the increased girth and, at times, increased length of the limb. The latter indicates an overgrowth of the bones and is found only when the lesion has been established for some time before the ossification of the epiphyseal cartilage, so that congenital cases are particularly liable to show it. The second effect is increase in superficial temperature, and the third, trophic changes. Pemberton and Saint (1927, p. 793) believe that the first two can be explained by the increased volume of blood flowing through the limb consequent upon the production of the fistula. They account for the trophic changes as being produced by two factors: First, the diminution of the flow of blood through the capillaries owing to its easier path of escape into the veins through the fistula, and second, the increased pressure on the veins impeding the return of deoxygenated blood from the capillaries. These two factors working together tend to bring about a state of anoxemia of the tissues affecting more particularly those most distally situated. On this account, if these tissues become even slightly injured, the normal inflammatory reaction necessary for their repair is either feeble or absent, and hence chronic progressive ulceration (partial obstruction) and later gangrene (total destruction) supervene. In their series in Cases 3, 5, 6, and 8, that is, all those in which an extremity was affected, chronic ulceration and gangrene were quite prominent features.

Bruits and thrills are found over the affected area in some cases. In 23 cases reported in 1932, Horton (1932, pp. 6, 7) found bruits present in 8 of the 23 cases, and thrills in 4 of these 8. By perfusing the arterial tree with water under a pressure of approximately 150 mm. of mercury in the amputated extremity in Case 1, Horton states that the bruit and thrill were reproduced and could be distinctly heard and felt in the region of the wrist. The arterial tree was injected with a mixture of sodium bromide and gelatin, and roentgenograms of the injected extremity were made. This illustrated abnormal communications between the arteries and veins. There were also some small communications in the bone itself. These observations were confirmed by dissection of the arm. There were also some small aneurysms in the arteries and veins similar to those previously described by Wilbur (1930).

The cause of the overgrowth of extremities, particularly the cause of the increase in length, is a subject of great interest. Horton (1934, pp. 460, 461) states that the increased flow of blood is the cause of the hypertrophy both of the bone and of the soft tissues. He states, also, that arteriograms of several subjects, the length of whose bones in the involved extremities had increased, revealed that the AVF's were adjacent to the epiphyseal line; whereas, arteriograms of three subjects without such increased length of bone in the involved extremities revealed that the abnormal communications between the arteries and veins were along

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may result in a hyperplasia of bone growth, according to Cone (quoted by Pearse and Morton). Studies on the blood changes in venous stasis made by Peters, Bulger, Eisenman, and Lee (1926) revealed an increase in the volume of the formed elements and increase in total plasma protein and an elevation of oxygen capacity and carbon dioxide content. The pH was reduced and relative acidity prevailed. The total acid and base of the plasma remained relatively constant while the salt content was apparently unchanged. Swindle (1935, p. 11) is of the opinion that the reduction of pH may be the factor which stimulates growth.

Harris and Wright (1930, pp. 142, 143) studied a case of heman-giectatic hypertrophy of the limb and made observations upon the rate of growth in the presence of increased blood supply in kittens who had been subjected to sympathectomy. These authors reported the case of a boy aged ten years with an overgrowth of the right leg. The right femur was 1 cm. longer than the left, while the right leg was 4.5 cm. longer than the left, most of the overgrowth of the extremity occurring below the knee. From the description given, it would seem that abnormal arteriovenous communications existed above the level of the knee. The authors assumed that there was an increase in the blood supply as a result of the AVF's. It would seem that the same conditions prevailed in this case as in other cases of abnormal venous communications with hypertrophy and that there was a venous stasis responsible for the overgrowth rather than an increase in blood supply. Cannon and others (1929) found that sympathectomy causes no change in the growth of long bones as compared with the normal side in kittens four months old. Harris and Wright (1930, pp. 147, 148), as a result of their experiments, also came to the conclusion that destruction of the sympathetic innervation of the forelimb of kittens with its resulting increased blood supply results in no increase in its bony structure.

The general or systemic effects depend on the disturbance in the function of the circulatory system produced by the development of the fistula and also on nature's efforts at compensation. Normally the circulatory system consists of heart, arteries, capillary bed, and veins. The formation of an AVF creates a new path through which the blood can flow, a second system, consisting of heart, artery, fistula, and vein being thus formed. The essential point of difference between the two systems is that the second (fistulous) system is practically devoid of peripheral resistance. Since a fluid will always flow along the path of least resistance, the less the peripheral resistance of the fistulous system, the greater will be the tendency for blood to pass through it. In order that blood may still continue to flow through the capillary system with its high peripheral resistance, it is essential that an adequate general blood pressure should be maintained (Holman, 1924, pp. 802, 803).

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Dry and Horton (1935, p. 661), in describing a case of spontaneous closure of a traumatic AVF involving the right femoral artery and vein, stated that "despite the fact that the fistulous communication was in the upper part of the thigh, the increase in bony growth was in the tibia rather than in the femur." Pemberton and Saint (1927, p. 793) also explain hypertrophy and increase in length of extremities as being due to an increased volume of blood flowing through the limb. On the other hand, they explain the trophic changes sometimes observed as due to the diminution of blood flow through the capillaries and the increase in pressure on the veins thus impeding the return of deoxygenated blood from the capillaries. These two factors, they believe, tend to bring about a state of anoxemia of the tissues affecting more particularly those most distally situated. Starling (1933, p. 1015) states that through the opening of the AVA's in the rabbit's ear the skin is flushed with warm blood so that its cooling is delayed. As Swindle (personal communication) has pointed out, the presence of AVA's or of abnormal fistulas has a tendency to shunt the blood directly into the veins and in that way to produce a decreased rather than an increased blood flow.

In the description of an arm which had been amputated because of changes resulting from AVF's, Pemberton and Saint (1927, p. 784) noted that upon injecting a solution opaque to Roentgen rays the solution returned almost immediately through the cut ends of the vessels. The solution filled the dilated proximal arteries and veins, the more distal vessels being only partially filled, because of the short circuiting due to fistulous communications. The stimulation of bone growth by venous stasis has been observed for many years. According to Pearse and Morton (1930), Ambroise Pare utilized stasis hyperaemia in order to stimulate the formation of callus. They state that later Nicoladoni advocated this method of treatment for the same purpose. In their survey of the literature on the effect of venous stasis upon bone growth, Pearse and Morton note that several observers have recorded clinical improvement in the repair of bone in the presence of venous stasis and that various authors have shown that any long continued inflammatory process which results in venous congestion will be followed by increase in the length and thickness of the bones. This response follows such causative factors as irritation of the periosteum, the introduction of foreign bodies, or the presence of a chronic ulcer of the leg in a young person. Pearse and Morton (1930) also state that the venous congestion resulting from arteriovenous aneurysms, angiectasis, and varicose veins may all produce a hyperplasia of bone. The passive congestion resulting from cardiac failure and the congestion of arteriosclerotic extremities

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lieve that for comparative work they are reliable. They have found that blood volume between 70 and 100 c.c. for each kilogram of body weight may be regarded as normal for different healthy individuals. On the other hand, the blood volume in the same healthy individual estimated at different times under comparable resting conditions may vary as much as 5 c.c. for each kilogram of body weight after ligation of the main arteries involved, a decrease greater than the normal variation. This single piece of clinical evidence, although supporting Holman's (1924) experimental results, does not justify any definite conclusions being drawn. However, these authors hope in due course to have the opportunity of studying blood volume in a sufficient number of cases to be able to satisfy themselves as to whether the data in this single case can be satisfactorily corroborated or not.

In many of the cases reported in the recent literature on the subject, enlargement of the heart has been noted, some times accompanied by symptoms or signs of myocardial degeneration (Pemberton and Saint, 1927). Until comparatively recently, it was thought that the heart condition was coincidental and that, if the state of the heart were poor, the surgical risk was correspondingly great and operation contraindicated. During the war, however, observers had the opportunity of studying a large number of cases, and they began to recognize that the condition of the heart was not coincident with, but consequent on, the production of the fistula. One of the most striking cases is reported by Leriche (1919). This surgeon extirpated an arteriovenous aneurysm in a case in which considerable cardiac enlargement and general signs of cardiac decompensation were present. The heart returned to its normal size and the signs of decompensation disappeared. This case, together with later abundant experimental work and clinical investigation by the Americans, Holman (1923), Reid (1925), Hoover and Beams (1924), and the Englishmen, Lewis and Drury (1923), has completely proved the detrimental effect of abnormal arteriovenous communications upon the heart. Opinions differ as to the cause of the cardiac enlargement. Lewis and Drury (1923) maintain that it is largely due to dilatation consequent upon faulty nutrition of the myocardium, the low diastolic pressure being insufficient to permit of adequate filling of the coronary vessels. On the other hand, Holman (1924), in experiments on dogs, found that in addition to dilatation there was an increase in the weight of the heart which he concluded must be due to hypertrophy. In Pemberton and Saint's series, cardiac enlargement was only demonstrable in two cases. It did not occur in any of Reid's (1925, *a*) cases.

An AVF has been described as analogous to an aortic leak, but, whereas in aortic regurgitation the left side of the heart alone undergoes dilatation and hypertrophy as a compensatory measure, in AVF both sides of the heart undergo these changes, the right side on account of having to cope with the increased intake consequent upon the abnormal



The systemic effects may be considered from three aspects: (1) peripheral resistance and blood pressure; (2) total volume of circulating blood; and (3) the reaction of the heart (Pemberton and Saint, 1927, p. 794).

While systolic pressure is chiefly maintained by cardiac output, diastolic pressure, on the other hand, is largely maintained by the elastic recoil of the arteries against the peripheral resistance. Following the production of a fistula the peripheral resistance is much diminished. Thus in AVF one would expect a normal or nearly normal systolic pressure and a low diastolic pressure, with consequent increase in pulse pressure. These are usually found, particularly in cases of the traumatic type. In 9 congenital cases reported by Pemberton and Saint, a low diastolic pressure was noted only in 3. On closure of the fistula (and, therefore, reestablishment of the normal peripheral resistance), the diastolic pressure rises to normal, while the systolic pressure usually remains about the same, although there may be a transient rise. Hoover and Beams (1924) reported that on closure of a fistula the systolic pressure rose by the same amount as the diastolic, but in most of the reported traumatic cases the systolic, as already mentioned, remains the same or rises only a few points. Owing to the multiple anastomoses present in congenital cases, these changes in blood pressure are difficult or impossible to elicit because of the difficulty of closing all of the fistulas simultaneously. Horton (1935, p. 460) states that the blood pressure was invariably higher on the involved side in cases of congenital AVF's.

Holman (1924, p. 802) has pointed out that because of the easier path of escape offered to the blood from the arterial system by an AVF, the amount of blood passing through the system, heart, arteries, capillaries, and veins is reduced according to the size of the fistula; that in order that the supply of blood through this system will be sufficient for the needs of the body, an adequate general blood pressure must be maintained; and that one of the compensatory mechanisms to insure this is an increase in the total volume of the circulating blood. He proved his theory to his complete satisfaction by experiments on dogs in which he had produced AVF's, showing that when the lesion was small (and, therefore, the amount of blood short-circuited back to the heart was correspondingly small) the blood volume remained constant or nearly so, while with larger fistulas he found a definitely increased blood volume together with changes in the heart and proximal vessels. Even admitting that the present methods for the determination of blood volume leave much to be desired, his results seem definite enough to be outside the limits of experimental error.

From a comprehensive study of blood volume (by the dye method of Keith, Rountree, and Geraghty) in health and disease, Brown and Rowntree (quoted by Pemberton and Saint, 1927) do not regard the results obtained by present methods of estimation as absolute, but be-

HCL and then for an hour or more in tap water. A more convenient method consists of injecting a 2 per cent or 3 per cent solution of HCL into the arteries and varying the injection pressure for many minutes. The tissue becomes edematous and loses its elasticity to such an extent that if a portion of it is compressed with a blunt object, such as a finger, this portion remains deformed for some time. Likewise, when the perivascular tissue is repeatedly forced aside by the walls of the rhythmically dilating vessels, it remains compressed for a sufficient length of time so that the veins, as well as the arteries, can be packed with cinnabar by injecting this substance in a rhythmic manner into the arteries. If no AVA's are present, cinnabar or India ink may be driven from the arteries into the capillaries, but not entirely through them into the veins, or the injected substance may be urged into the veins through the capillaries. Cinnabar can rarely be packed firmly enough in the capillaries for these vessels to be visible in photomicrographs. Very slender columns of India ink in the lumen of the capillaries can be demonstrated much better photographically than the slender columns of cinnabar in the lumina of these vessels.

#### IV. DIRECT OBSERVATIONS

A. *Injected Blood Vessels.*—In the laboratory studies of injected blood vessels, AVA's were found in the ears of the rabbit, timber wolf, coyote, kangaroo, and dog (see Figs. 1 and 2); the stomach of the human fetus (Swindle, 1935); the tunica albuginea of the prong-horned antelope; and the Scotch buck (Dysach, unpublished material). No AVA's were found in the mucous linings of the nasal passages of any of the mammals examined; in the human liver or gallbladder or in the capsule of the dog's kidney. They were not found in the injected specimen of the swan's foot, but this preparation was not entirely satisfactory so that our failure to demonstrate them in this tissue cannot be interpreted as meaning that they did not occur. AVA's were found in these tissues in a number of varieties. Funnel shapes were frequent in the rabbit's ear, but not so common in the other tissues. In the ear of a dog whose body had been cooled with ice water before death, there was marked contraction of the AVA's (Fig. 2) as compared with those found in the ear of another dog whose death occurred at normal room temperature (Fig. 1).

#### B. *Clinical Observations.*—

CASE 1.—The patient, a white male, aged nine years and five months, was admitted to the Milwaukee Children's Hospital on March 18, 1935, because of swelling of the right leg. Two and one-half years before admission he had injured the right leg when he jumped off a stump. Following this accident, the right ankle was swollen and painful. The father assumed that the ankle was sprained. The swelling diminished very slowly, and the ankle never returned to normal size. Since the accident the ankle has become larger during the day when he is active and the

escape of blood into the veins through the fistula, the left side in order to increase output to maintain adequate general blood pressure. If Holman's contention be correct, in addition to these factors, the heart has to deal also with increased total volume of blood.

Lewis (1930, p. 18) states that while Branham is given credit for noting that in closure of an AVF slowing of the pulse rate is produced, and this observation has since been spoken of as Branham's bradycardiac phenomenon, this sign was described by Nicoladoni fifteen years before it was noted by Branham. He states that, however, Nicoladoni did not describe the lesion as a congenital arteriovenous aneurysm. It could not be elicited in any of the congenital cases in Pemberton and Saint's (1927, p. 796) series because of the difficulty in closing the multiple communications.

### III. MATERIALS AND METHODS USED IN THIS INVESTIGATION

An intensive study was made of a clinical case presenting features of congenital AVF's. Clinical studies included x-ray examination, arteriography, infra-red photography, skin surface temperatures, careful measurements, and studies of the oxygen content of the blood in the affected and sound sides. Laboratory studies of various injected tissues were made. These tissues were prepared and injected by Dr. P. F. Swindle, India ink and cinnabar suspension being used. The injected tissues were cleared by the Spalteholz method and in some instances decalcification with HCL was employed. The tissues were examined with the binocular microscope. Among the tissues studied were the following: human liver and gallbladder; foot of a swan; penis of prong-horned antelope and Scotch buck; stomach of human fetus; turbinate of reindeer; ears of the rabbit, timber wolf, kangaroo, coyote, dog, and antelope; capsule of the dog's kidney.

The Spalteholz method consists of dehydration of the tissues with absolute alcohol, displacing the alcohol with benzine, the benzine then being displaced with synthetic oil of wintergreen. The arteries were injected first with India ink and then with red cinnabar suspension. By this method the ink is driven into some of the capillaries only or into the capillary venules and veins. If the cinnabar is not firmly packed into the arteries, some of the ink may remain in some of the smallest arteries. The amount of ink passing into and beyond the capillaries may depend upon the amount of ink injected as well as upon the amount of cinnabar packed in the arteries. Under certain conditions, an abundance of cinnabar can be urged through the capillaries and into the veins. According to Swindle, this can be accomplished best by first diminishing the elasticity of the perivascular tissue while the intravascular fluid pressure is being altered in a rhythmic fashion. The pulsatile variations in the vessels may be produced while the tissue is placed for several seconds in a moderately concentrated

clavicular line. There is a faint systolic bruit at the apex which is not transmitted. There is no thrill present. The rate is normal. Except for its prominence, the abdomen is negative. The right lower leg is larger than the left. There is some edema about the right ankle. The superficial veins are prominent on the right and become markedly engorged on standing. The entire right lower extremity becomes slightly dusky in color when the patient is erect. The upper extremities are equal in size. The superficial arteries of the arms and legs are palpable and apparently equal bilaterally. No thrills or bruits are present over the arms or legs. The skin temperature of the right leg is grossly higher than that of the left. Detailed studies



Fig. 2.—Photomicrographs showing typical AVA's in dog's ear. The method of injection is the same as that used for Fig. 1. This animal's body had been exposed to ice cold water immediately before death. The insert represents the area within the circle of the large photograph. The magnification of the large photograph is 27.6, that of the insert is 69. Reflected light only was used in photographing the insert, while the large photograph was made with reflected and transmitted light. Note the exaggerated contraction of the AVA's in this figure in comparison with those shown in Fig. 1.

of skin temperature readings are given in following tabulations. Routine examinations of the blood and of the urine were essentially negative. The blood pressure was as follows: right arm, 110/60; left arm, 105/60; right leg, 130/80; left leg, 120/80.

On March 18, 1935, 10 c.c. thorium dioxide solution (thorotrast) was injected into the right femoral artery with compression of the artery above the site of in-

swelling has subsided somewhat at night. For several months following the accident, the ankle ached considerably. He has been wearing a high boot in order to prevent the swelling during the day and finds that this has been of some benefit to him. The veins of the right leg have been observed to be somewhat larger than those of the left leg. No swelling was noticed prior to the accident.

The patient's general health has always been good. Aside from draining ears at various times during the past six years, his past history for acute diseases is essentially negative. At the age of nine years he was in grade 3-B, and the father thinks his mental development is average. The father is well. The mother died in



Fig. 1.—Photomicrographs showing typical AVA's in dog's ear. India ink was injected into the carotid artery and this was driven over into the capillaries, AVA's, and veins by injecting cinnabar suspension into the same artery. The magnification of the large photograph is 103.9 and of the insert, 27. Reflected light only was used in making these pictures. A, artery; V, vein; AVA, arteriovenous anastomosis.

1927 following an abortion. There are three living children in the family, aged twelve, nine, and eight years. The other two children are well.

The patient is a thin, fairly well-developed boy. He is round shouldered and assumes a fatigued posture. The abdomen is prominent. He walks without a limp. He is alert and cooperative. Aside from the presence of a perforation in Shrapnell's membrane on the right, examination of the head and neck is essentially negative. The chest is symmetrical except for the suggestion of a pigeon breast. His heart is within normal limits, the apex being in the fifth interspace, 1 cm. within the mid-

clavicular line. There is a faint systolic bruit at the apex which is not transmitted. There is no thrill present. The rate is normal. Except for its prominence, the abdomen is negative. The right lower leg is larger than the left. There is some edema about the right ankle. The superficial veins are prominent on the right and become markedly engorged on standing. The entire right lower extremity becomes slightly dusky in color when the patient is erect. The upper extremities are equal in size. The superficial arteries of the arms and legs are palpable and apparently equal bilaterally. No thrills or bruits are present over the arms or legs. The skin temperature of the right leg is grossly higher than that of the left. Detailed studies



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of skin temperature readings are given in following tabulations. Routine examinations of the blood and of the urine were essentially negative. The blood pressure was as follows: right arm, 110/60; left arm, 105/60; right leg, 130/80; left leg, 120/80.

On March 18, 1935, 10 c.c. thorium dioxide solution (thorotrast) was injected into the right femoral artery with compression of the artery above the site of in-

The vein was bifurcated at this point. The artery profunda femoris was ligated below the second perforating branches. This produced marked diminution in the size of the vein.

There was little change in the local condition following this operation, and on October 7, 1935, the popliteal artery and vein were exposed and thoroughly examined. No communicating fistulas were found. There were numerous small branches coming off of both the artery and vein. These were ligated and cut.

The boy's recovery following both surgical procedures was uneventful and while he remained in bed there was considerable diminution in the size of the leg, but the induration in the soft parts below the knee did not entirely disappear. The x-ray showed definite thickening of the soft parts of the right leg and thigh. There were many dilated veins visible on the calf of the right leg, especially on the lateral aspect.

The skin surface temperatures and the measurements of the lower extremities taken at various times are as shown in Table I.

TABLE I

March 18, 1935; Temperature				Right	Left			
Arm				34.8° C.	34.4° C.			
Forearm				34.6° C.	24.2° C.			
Thigh				35.4° C.	34.6° C.			
Calf				35.0° C.	34.6° C.			
Gluteal fold				36.2° C.	35.0° C.			
Popliteal space				34.6° C.	34.6° C.			
Foot				33.4° C.	32.4° C.			
Measurements				Right	Left			
Circumference 24 cm. above thigh				36.5 cm.	34.2 cm.			
Circumference 17 cm. below knee, calf				26.6 cm.	23.5 cm.			
Circumference ankle				24.6 cm.	23.0 cm.			
Circumference arm				17.0 cm.	16.8 cm.			
Circumference forearm				17.5 cm.	17.2 cm.			
Length anterior superior spine to internal malleolus				75.5 cm.	75.5 cm.			
Length knee to internal malleolus				36.6 cm.	36.6 cm.			
Measurements	3-14-35	4-25-35	7-11-35	9-9-35	9-24-35	10-31-35	11-26-35	
Right ankle	7.6 cm.		20.0 cm.	18.5 cm.	20.0 cm.	20.5 cm.	20.5 cm.	
Right calf	26.8 cm.	28.0 cm.	27.0 cm.	26.0 cm.	27.0 cm.	26.0 cm.	28.0 cm.	
Right knee	30.8 cm.		31.0 cm.	31.6 cm.	32.5 cm.	34.0 cm.	38.0 cm.	
Right thigh	34.0 cm.	36.2 cm.	34.0 cm.	34.5 cm.	36.5 cm.	34.0 cm.	38.0 cm.	
Left ankle	7.6 cm.		17.0 cm.	17.0 cm.	17.0 cm.	16.5 cm.	17.0 cm.	
Left calf	24.0 cm.	25.0 cm.	24.0 cm.	23.0 cm.	24.0 cm.	23.5 cm.	25.0 cm.	
Left knee	29.2 cm.		29.5 cm.	29.5 cm.	30.5 cm.	29.5 cm.	30.5 cm.	
Left thigh	30.3 cm.	33.1 cm.	31.5 cm.	33.0 cm.	34.0 cm.	33.0 cm.	35.5 cm.	
Temperatures	8-10-35		9-9-35		9-24-35		11-7-35	
	Right	Left	Right	Left	Right	Left	Right	Left
Arm	35.0°	34.0°	35.2°	35.2°	35.0°	35.2°	35.4°	35.5°
Forearm	35.2°	35.0°	35.2°	35.4°	36.6°	36.0°	35.3°	35.4°
Hand	35.4°	35.0°	35.4°	35.4°	36.0°	35.8°	35.8°	35.6°
Thoracic	34.8°	35.0°	35.4°	35.2°	35.8°	36.0°	35.4°	35.0°
Lumbar	34.6°	35.0°	34.6°	34.6°	36.2°	36.2°	35.0°	34.4°
Temperatures	8-10-35		9-9-35		9-24-35		11-7-35	
	Right	Left	Right	Left	Right	Left	Right	Left
Thigh:								
Anterior			35.4°	35.2°	35.8°	35.0°	36.0°	35.8°
Posterior	35.2°	35.0°	35.0°	35.0°	36.2°	36.0°	34.4°	34.0°
Calf	36.0°	34.4°	34.2°	34.0°	36.4°	35.6°	34.2°	32.0°
Popliteal	35.0°	34.6°	35.4°	35.0°	36.4°	36.2°	34.3°	33.6°
Gluteal	35.6°	36.0°	37.0°	36.0°	37.2°	36.2°	35.9°	35.4°
Patellar			36.6°	33.6°	36.6°	35.2°	36.2°	35.4°

CASE 2.—A white female, aged eight years, was seen in consultation with Dr. Walter P. Blount on January 20, 1936. This child complained of a small left leg. The discrepancy in size of the left leg was noticed by the child's father, who is a physician, when the child was six weeks old. No history of injury or of contagious disease could be elicited. Recently the discrepancy between the right and left legs had become more noticeable. There was no history of pain in the extremities. Examination of the pelvis and both lower extremities was negative except for the increase in length of the bones of the right leg. The measurements are shown in Table II.



Fig. 5.—Infra-red photograph of child with hemihypertrophy involving the right leg. The absence of abnormalities of the veins of either leg is well demonstrated by this method and is of definite value in eliminating the presence of arteriovenous fistulas.

The right foot was at least 1 cm. different in length from its fellow. When standing on a  $\frac{3}{4}$ -inch elevation under the left foot, the pelvis was level and symmetrical. Standing in bare feet, there was a left total scoliosis. The left arm hung away from the side, while the right hung next to the body. There was moderate pronation of both feet, which was not excessive. There was no difference in temperature of the legs on palpation, except over the knee where the right was warmer. X-ray pictures, anteriorposterior of the lower extremities, revealed no



TABLE II

	RIGHT	LEFT
Forearm		
Upper arm	20.6 cm.	20.4 cm.
Length of arm from the acromion to the radial styloid	22.6 cm.	21.3 cm.
Circumference of calf (standing)	44.0 cm.	44.0 cm.
Circumference of thigh (standing) 15 cm. above the patella	35.0 cm.	30.8 cm.
Length of leg	48.5 cm.	44.2 cm.
Circumference of calf with legs elevated	74.2 cm.	71.0 cm.
Circumference of thigh (relaxed) 15 cm. above the patella	34.2 cm.	30.5 cm.
Length of tibia	48.0 cm.	43.5 cm.
Length of femur (measured obliquely)	32.0 cm.	31.0 cm.
	42.0 cm.	41.0 cm.

difference in the conformation of the long bones, which in the right were larger in every way than the left: right tibia, 32.5 cm.; right femur, 41.5 cm.; left tibia, 31.5 cm.; and left femur, 39.0 cm. The ischiopubic synchondrosis on the right was enlarged and not completely closed. That on the left was completely closed. Otherwise the epiphyses on the two sides were symmetrical and the bones were negative for radiologic changes.

This child was examined by means of infra-red photography which revealed no dilatation of the deep veins (Fig. 5). This method was of assistance in eliminating the presence of abnormal communications between the arteries and veins in this case. The final diagnosis of hemiphyertrophy of the right leg was decided upon because of the absence of any abnormality of either leg other than the difference in size.

#### V. GENERAL DISCUSSION

The relative rarity of congenital AVF's in clinical medicine is noteworthy in view of the development of the blood vessel system. The origin of the arteries, veins, and capillaries from a common bed not only explains the occurrence of these fistulous communications, but makes their infrequent occurrence worthy of comment. As Sabín (1917, p. 120) has noted, in certain embryonic vessels the direction of the flow of blood may be reversed so that these vessels which function as arteries during one stage of development, function as veins during another. Woolard's (1922) plates show clearly the capillary network through which the forelimb bud of the pig embryo first gets its blood supply, and how, at a later period, when subclavian artery and vein are beginning to be differentiated, there are numerous communications between the two vessels. Reid (1925, *b*) expresses wonder at the fact that pathologic varieties of AVA's do not occur more frequently. Swindle's (1935, p. 8) observation that some embryonic AVA's are fixed by solid tissue about them so that they cannot loop away and develop normally is worthy of considerable thought. It has some clinical support in the fact that Lewis (1930) reported a case of congenital AVF's involving the ear, and that several cases have been reported in which large arteriovenous communicating channels have occurred in bone. It is probable that since our attention has been directed to this subject by the work of Halsted (1919), Reid (1925), Pemberton and Saint (1927), and Horton (1931), more

cases will be recognized. The relative increase in the number of cases seen at the Mayo Clinic within a few years would tend to substantiate this statement.

The method of development of the blood vascular system is of interest, not only as providing an academic background for an understanding of this subject, but also because it helps to throw some light on the nature of the processes sometimes seen in clinical medicine. The essential similarity between various types of blood vessel tumors and AVF's has been commented upon previously in this thesis. Reid's (1925, b) statement that there is a basic similarity between cirroid aneurysms and arteriovenous aneurysms is particularly interesting. Trauma is a common factor in both and he believes that angiomas, cirroid aneurysms, and arteriovenous aneurysms have the same etiologic basis. Trauma was an important factor in the history of the case presented here and is noted in many clinical reports. Lewis (1930) states that trauma is by far the most frequent cause of arteriovenous aneurysms, and the history of injury in many of the cases in the literature seems to be more than coincidental. It is probable that some anomaly in the blood vascular anlage permits the development of this lesion, when some causative factor, such as trauma, may result in spontaneous communications between the arteries and veins. Horton and Ghormley's (1935, p. 141) observation of the appearance of an arteriovenous communication in the leg following obliteration of a congenital fistula in the thigh is also of interest in this regard, as it illustrates the probable existence of a preformed channel which had not become clinically apparent. Clark and Clark's (1934, p. 239) observation that new AVA's appeared in a region which had been submitted to extensive study for many months is also significant in considering the clinical aspects of these cases. In applying our knowledge of the genesis of the blood vessels to this subject, one is safe in assuming that the preponderance of evidence favors the principle of the local origin of intraembryonic endothelium from mesenchyme. McClure, in his address as President of the American Association of Anatomists in 1924, stated that the angioblast theory as proclaimed by His no longer holds and voiced his belief that the theory of local genesis of endothelium is an established fact. This statement was especially significant in view of the controversy which had raged for years in the American Association and among European anatomists regarding this subject. McClure's views have not been challenged in the literature since that time and they undoubtedly represent the conclusions of the anatomic world today.

The disappointing lack of accurate knowledge of the anatomy of the capillaries is evidenced by the meager reference made to these structures in standard textbooks on anatomy and the lack of special works on this subject. The monograph of Krogh (1929) stands almost alone in the academic field, while Brown (1926, 1929, 1935), of the Mayo Clinic,

working in clinical medicine, has made, in recent years, important contributions to our knowledge of these structures both in normal and abnormal subjects. It is evident from the studies of these two men that there is a great variation in the capillaries so that an approach to this subject, with a view of determining the effect of pathologic communications, is hampered by a lack of accurate knowledge of the normal. The possibility that the blood may not be limited by walls of endothelium in some regions, as for instance in the spleen, further complicates the picture.

The existence of AVA's is generally accepted. These derivating channels are not to be confused with the pathologic AVF's of gross anatomy. Krogh's (1929, p. 103) statement that, though wider than arteries when fully dilated, AVA's are much too small to be seen with the naked eyes and cannot in any way imperil the circulation even when present in very large numbers, is significant in view of the inadequate state of our knowledge regarding the anatomy and physiology of these structures. Clark and Clark (1934, p. 281), from their studies, conclude that without question the changes of blood flow and the oxygen content of the venous blood from regions in which these structures are numerous must be greatly modified. The lack of clearly defined limits between what may be considered normal and what is to be considered pathologic when arteriovenous communications occur independent of a capillary bed is at once apparent. The earlier work of Hoyer (1877) has been confirmed in part by Grant (1930), Grant and Bland (1931), Clark and Clark (1934), and Swindle (1935). The observations here recorded also tend to confirm some of the earlier reported work. However, the opinion of Swindle (personal communication) that one cannot accept too freely earlier statements relative to the existence of AVA's, and his emphasis on the necessity of studying further their distribution must be kept in mind before any conclusions are accepted. Grant and Bland (1931, p. 406) also voice the opinion that much of the earlier work on AVA's needs confirmation. In this connection it should be noted that in the literature it is stated as an accepted fact that AVA's are present in the corpora cavernosa. Swindle and Dysach (personal communication) have not been able to confirm the presence of AVA's in the corpora cavernosa of several animals examined, but they have found numerous AVA's in the tunica albuginea in the prong-horned antelope and Scotch buck.

The evidence relating to the function of AVA's is conflicting and it would seem that thought regarding these structures is somewhat confused. While AVA's are usually credited with increasing the blood flow to a part, a consideration of the anatomic arrangement would lead one to believe that in some instances a decrease in the amount of blood flowing through a region might occur because of the short-circuiting effect of these structures. The wide variation in the reaction to various stimuli is well demonstrated by the works of Grant (1930) and of Clark and

Clark (1934). A perusal of the literature merely emphasizes Grant's (1930, p. 280) statement that we have no experimental evidence of the function of AVA's.

In considering the regional changes produced by the pathologic varieties of arteriovenous communications, the cause of the overgrowth of extremities is especially interesting. It is obvious that there is no unanimity of opinion regarding the basic nature of the process responsible for this phenomenon. In all of the cases described, increase in length occurred only when abnormal communications existed for a considerable time before ossification. Clinicians generally dismiss the subject by the statement that the increase in length is due to an increase in the local blood supply. Tending to prove this point, Horton (1934, p. 461) has reported on arteriograms of several subjects, the length of whose bones in the involved extremities had increased, revealing that the AVF's were adjacent to the epiphyseal line. In three subjects without such increase in length of bone in the involved extremities, the abnormal communications were along the shafts of the bones. Dry and Horton (1935) describe a case of spontaneous closure of a traumatic AVF involving a right femoral artery and vein and state that "despite the fact that the fistulous communication was in the upper part of the thigh, the increase in bony growth was in the tibia rather than in the femur." Pemberton and Saint (1927, p. 793) also explain hypertrophy and increase in length of extremities as being due to an increased volume of blood flowing through the limb. On the other hand, they explain the trophic changes sometimes observed as due to the diminution of blood flow through the capillaries and the increase in pressure on the veins, thus impeding the return of deoxygenated blood from the capillaries. It is probable that rather than being due to an increase in blood supply, overgrowth is due to passive hyperemia and to the presence in the extremity of relatively deoxygenated venous blood. The references to the stimulation of bone growth by venous stasis previously referred to, and which is well recognized clinically, would tend to confirm this point. Further confirmation is found in the work of Cannon and others (1929), in which an increase in the blood supply to the extremities of kittens following sympathectomy did not result in an increase in growth of the long bones. In the case reported by Harris and Wright (1930), the increase in the length of the leg occurred mainly below the point of the AVF's. Here the authors also assumed that the increase in length was due to an increase in blood supply; whereas, venous congestion would seem to be a more reasonable interpretation. That the increase in length and the hypertrophy of the tissues are due to a change in the blood supply rather than some other factor is supported by physiologic thought. Claude Bernard (quoted by Cowdry, 1928, vol. 1, p. 3), called the interstitial lymph, in which cells are immersed, the *milieu intérieur*. This great physiologist believed that the metabolic condition of the cells de-

pended on the composition of this medium. Alexis Carrel (quoted by Cowdry, 1928, vol. 1, p. 3) states that the quantitative and qualitative reactions of the tissues to the physical chemical conditions of the inter-organic medium are responsible for the harmonious growth of the body. The cell metabolism and morphology depend on the quantitative and qualitative characteristics of the humors.

The short-circuiting of the circulation because of AVF's has a tendency to produce a venous stasis in the peripheral portions of the extremity involved, with a consequent lowering of the pH of the blood. The statement that there is an increase in blood supply can hardly be supported by the evidence at hand and does not seem to be in accord with the anatomic arrangement of the described anastomoses.

The studies of Peters and others (1926) revealed, among other changes, a reduction in the pH of the blood and the existence of relative acidity following upon venous stasis. Swindle (1935, p. 11) is also of the opinion that the reduction of the pH may be the most important factor in the stimulation of bone growth and soft tissue growth in these cases.

The observations on laboratory materials tended to confirm the observations on living AVA's in the rabbit's ear made by Clark and Clark (1934) and of observations of Grant (1930) made on the same tissue in injected and living preparations. It should be pointed out that the morphology of AVA's as described is varied and that not all varieties are found in every tissue. For instance, funnel types are more frequent in the rabbit's ear, while this was not the case in other tissues examined. Krogh (1929, p. 101) makes the criticism of the injection method that it does not lend itself to verification by a study of the structures of the vessels in question. In addition, he believes that single capillaries can easily become greatly dilated by injection under pressure and give the appearance of wide channels so that he thinks evidence of this kind is untrustworthy. Swindle (personal communication) believes that, with the method as used by him, this criticism is purely an academic one. Swindle believes that artifacts suggesting AVA's may be seen in injected specimens because of compression of veins by arteries. He states that he has never seen inflated capillaries following the proper injection of tissues except in cases where the blood vessels are hypertrophied. In the specimens injected and cleared by Swindle in which AVA's were seen, the evidence of the nature of these structures seemed so clear as to leave little room for argument.

The use of arteriography in the demonstration of AVF's promises to aid considerably in the diagnosis and treatment of this condition. In the case reported here the method did not enable us to localize the fistulas and it is probable, because of the nature of the congenital communications, their small size, and great numbers, that the method will be of limited usefulness. The possibility of this method being of value in the diagnosis of the existence of AVF's should be borne in mind when lesions occur in the extremities. The use of arteriography in the demon-

stration of AVF's occurring intracranially does not seem to be warranted because of the dangers attending the use of a contract medium in this region. The dangers apparently outweigh the value to the patient of any added evidence which may be so obtained. The dangers associated with the injection of large quantities of thorium dioxide are well recognized. The amount given in this case (thorotrast, 28 c.c.) is well within the limits and is considered as safe. Failure to demonstrate large communications or communications in association with the large trunks in the reported case do not negative the diagnosis. The diagnosis, in this case, rests upon the hypertrophy of the leg, the presence of dilated veins containing arterialized blood, and the increase in local skin temperatures.

The value of infra-red photography in the differential diagnosis of hemihypertrophy of the extremity is evident from the case here reported. The absence of dilated veins below the surface of the skin in the case of hemihypertrophy helps to exclude the presence of arteriovenous fistulas. The markedly dilated and tortuous veins demonstrated in the case of AVF's is important added evidence in establishing that diagnosis. Its use for this purpose has not previously been reported.

#### VI. SUMMARY AND CONCLUSIONS

A review of the literature indicates that the *in situ* theory of vasculogenesis is generally accepted among anatomists. The assumption generally held by physicians that our knowledge of the capillary bed is accurate and complete is incorrect. A resume of our knowledge concerning the capillaries is given here as a background for the discussion of the clinical phenomena observed in congenital AVF's. Our knowledge of the anatomy and physiology of AVA's is reviewed for the same purpose. Laboratory observations of injected blood vessels have been made in order to supplement the studies of clinical cases. These laboratory studies, in the main, supported the observations of Clark and Clark (1934), Grant (1930), and Grant and Bland (1931), previously referred to in this thesis. The presentation of a case of AVF's and a case of hemihypertrophy of undetermined origin involving the lower extremity demonstrates the value of infra-red photography as an aid in the differential diagnosis of hemihypertrophy of the extremities. The oxygen content of the blood, the increased temperature of the skin of the involved extremity, the venous dilatation, and hypertrophy of the soft tissues established the diagnosis of arteriovenous fistulas. Arteriography did not aid either in establishing the diagnosis or in locating the site of the fistulous communications in the case here reported.

On the basis of these studies the following conclusions have been arrived at:

1. The *in situ* theory of vasculogenesis is generally accepted as in keeping with observed facts.
2. Our knowledge of the anatomy of the capillaries is inadequate.

pended on the composition of this medium. Alexis Carrel (quoted by Cowdry, 1928, vol. 1, p. 3) states that the quantitative and qualitative reactions of the tissues to the physical chemical conditions of the inter-organic medium are responsible for the harmonious growth of the body. The cell metabolism and morphology depend on the quantitative and qualitative characteristics of the humors.

The short-circuiting of the circulation because of AVF's has a tendency to produce a venous stasis in the peripheral portions of the extremity involved, with a consequent lowering of the pH of the blood. The statement that there is an increase in blood supply can hardly be supported by the evidence at hand and does not seem to be in accord with the anatomic arrangement of the described anastomoses.

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3. AVA's exist in various tissues as physiologic structures.
4. The function of physiologic AVA's is not known.
5. The relatively rare occurrence of congenital arteriovenous fistulas is noteworthy in view of the development of the blood vascular system.
6. Infra-red photography is of definite value in the differential diagnosis of the cause of hemihypertrophy of the extremities and as an aid in the diagnosis of arteriovenous fistulas.
7. The cause of the increase in length of bones and of hypertrophy of tissues in congenital AVA's is not known. It is probably due to venous stasis and the resulting decrease in the pH of the blood.

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The urine does not appear always to be changed as the author has seen dying patients with extensive burns and a normal excretion of urine. He calls attention to the fact that if there exists urinary retention these patients will respond very well to diuretics. The polypeptids and the amino acids are increased. The author notes the presence of creatine in the urine and the presence of an abnormal increase of creatinine. Glycosuria is frequent. Like Goiffon, he was able to demonstrate the presence of sodium bicarbonate in the urine towards the third to the fourth day.

The pathogenesis is explained by the author as the following: The heat in attacking the tissue albumin produces a quantity of highly toxic proteins which are carried by the veins to the entire body. The quantity is proportionate to the mass of tissue destroyed. Thus, the local lesion can become generalized because of the toxic substance produced in the involved area and carried to the remainder of the organism by the blood stream. Evidence of the breaking down of the albuminoids is the increase of toxic substances in the blood such as polypeptids and uric acid. This toxic stage lasts, in general, until the fourth to the sixth day. It ends in death or by gradual return to recovery. The methods of body defense are the following: (1) the liver destroys certain toxic substances such as the polypeptids by transforming them into urea; (2) the lungs excrete amino acids; (3) a certain proportion of the toxic substances is eliminated in the urine; and (4) fixation of the blood chlorides.

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**I. The General Treatment.**—Combating the toxemia. For pain the author recommends morphine except in infants for whom codeine or chloral is preferred. Heat should be applied to the patient and substances should be given to combat the hypotensive collapse (author prefers ephedrine). To combat the increase of blood concentration due to the enormous loss of fluid in the region of the burned area resulting from an abnormal permeability of the capillaries, it is necessary to resort to intravenous injection of isotonic saline (4 to 5 L. per day appear sufficient). It is necessary to combat the hypochloremia (in accord with the investigations of Davidson) and the increase in polypeptids of the blood by giving 100 c.c. of hypertonic saline (10 per cent) daily. Blood transfusion is often useful. The author prefers repeated small transfusions of 200 to 300 c.c. The presence of toxic granulations of

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(From the Faculty of Medicine, Strasbourg, France, and the Surgical Clinic of  
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**PIERRE DUVAL** (Paris), and **Mourgues-Molines** (Montpellier): *The Pathologic Physiology and Treatment of Recent Extensive Cutaneous Burns.*—The authors refer to extensive burns as those belonging to the second and third degree groups, according to Dupuytren's classification (vesicle formation and necrosis), involving at least one-third of the cutaneous surface, during the period of intoxication between the fourth and tenth days.

**Pierre Duval** (in collaboration with **J. C. Rudler**): *I. Physiopathology.*—The author calls attention first to the frightful mortality of extensive burns and to the fact that the seriousness of the burn varies in direct proportion with the calculated involvement of the body surface. He adopts for this calculation the table of Berkow. The personal statistics of the author are based upon 16 observed cases in six months. Fifteen died, 60 per cent dying in the first six to twenty-four hours.

*II. The Clinical Picture.*—This is described as essentially a period of excitation (agitation, mental disorientation, convulsions) followed by a period of somnolence which ends in coma (with myosis and Cheyne-Stokes' respiration) and death. Emaciation appearing on the fourth to the fifth day is a bad prognostic sign. The blood pressure is generally low and the pulse is very rapid. Urine is scanty, although occasionally it is normal in quantity. The temperature is not infrequently low at the onset. On the third or the fourth day there sometimes appears a marked hyperpyrexia which the author explains by the particular action of the circulating toxins in the blood on the central thermal regulating center.

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**Hamant** (Nancy) and **Grimant** (Algrange) reported on their interesting observations in which they resorted to the immediate excision of the burned region.

**Yves Bourde** and **Roger Gary** reported on 25 cases of burns which they studied. They called attention to some cases of burns in children who have presented a syndrome very similar to the syndrome of hyperpyrexia of nutrition. They advocated in these instances the use of cold applications. In the infected cases they resort to mercurochrome.

**P. Lombard** and **Montpellier** (Algeria) reported on the histologic findings of two interesting observations. In the first case a child of seven years of age having a burn occupying more than 50 per cent of the body surface died twenty-seven hours after the accident. Histologic examination disclosed only lesions of the tubules of the kidney. On the other hand, in the second case, which was a child of twelve years of age having a normal blood nitrogen, they noted a characteristic glomerulo-nephritis. They also noted degenerative lesions of the liver.

**Paul Piollet** and **H. Limousin** (Clermont-Ferrand) have employed vitamin A. which they believe diminishes the toxicity and favors cicatrization. In some cases they first applied mercurochrome and then compresses of cod liver oil.

**Yves-Delageniere** (Le Mans). These authors still employ alcohol dressings which was taught them by their former chief, Lecene, and which they employ under anesthesia of ethylene chloride. They call attention to the fact that the practicing physician, nurses, attendants, etc., should be instructed against the immediate application of oil or grease in cases of burns. The manuals of first aid should be corrected in this regard and advocate dry sterile dressings as the best immediate form of therapy before sending the patient to the surgical service.

**Chevallier** and **Carcassonne** (Marseilles) reported very favorable results with the use of vitamin A. They believe that it favors cicatrization and elasticity of the scar, which they believe is important, especially in the region of the articulations.

**J. Fiolle** and **T. Funck-Brentano**: **Arterial Emboli of the Extremities—Physiologic Pathology and Treatment.**

**J. Fiolle**: **The Physiological Pathology of the Arterial Emboli of the Extremities.**—After having rendered respect to the work of René Leriche, the author then discussed "lost" (*manquée*) emboli and "occult" emboli. The "lost" (*manquée*) emboli are those which, after having a sudden and dramatic onset, go on toward recovery without having provoked gangrene. The "occult" emboli are those which are not suggested by any signs indicative of embolus. These types are of interest, because they may indicate a possible mechanism of defense.

The author referred to the possible origin of emboli (thrombi originating from the heart or aneurysm, atheromatous plaques detached from an arterial wall). The author with his student, Haimovici, found that septic emboli play a most important rôle in coagulation. Whereas in 10 experimental aseptic emboli there was no important thrombosis except a clot of 2 or 3 cm., of 7 septic emboli in the dog there was extensive thrombosis extending towards the periphery from the point of obstruction.

The parietal lesion in the region of the embolus involves the intima (epithelial desquamation), very little of the media, but especially the adventitia (active endo-



Fasal indicates the practicability of transfusions. The usefulness of convalescent serum is not established. The author refers to the good results obtained by Wilson by the administration of large doses of suprarenal cortex extract.

**II. The Local Treatment.**—The author makes a detailed study of this. A careful disinfection of the wound should be done first as was indicated by Nageotte-Wilbouchewitch in 1893. The author refers in detail to the different methods utilized in combating the intoxication, such as excision (which the American authors designate under the term “*débridement*” which is actually incorrect), or the method of continuous baths of Hebra (Wasserbett), or the method of desiccation of the burned surface by the exposure to free air. He considers the tannic acid method of Davidson as the best. He reports in detail the history, the technique, and the excellent result. As successors of tannic acid, he mentions silver nitrate, perchloride of iron, gentian violet, mercurochrome, and brilliant green.

The author states that the following methods are advocated to stimulate cicatrization after the removal of the tannate crust: wet compresses of Dakin's solution, local application of cod liver oil, and ultraviolet rays. In conclusion the author proposes tannic acid as the most rational type of treatment, except in burns of the face which heal very well by simple exposure to air.

**Discussion.**—**McClure** (Detroit), by invitation of the Congress, showed a beautiful film from the Henry Ford Hospital demonstrating the manner in which the tannic acid treatment is practiced there. Some patients with 55 per cent of the body surface burned have recovered.

**Riehl** (Vienna), invited by the Congress, stated that he treated burns with transfusions without tannic acid. Sixty per cent of the burned cases recovered. After a discussion on the morphologic modifications of the blood, he spoke on the treatment by continuous baths (Wasserbett) originated by Hebra, Vienna, which had certain advantages, particularly the preservation of articular mobility.

**Wilson** (Edinburgh), invited by the Congress, stressed the usefulness of cortin to combat the toxemia.

**Von Seemen** (Munich), invited by the Congress, suggested the use of the electro-surgical unit in the burned region for its mechanical cleansing effect, and added that after clinical and experimental investigations he noted a marked diminution of the absorption of toxic products.

**Mario Donati** (Milan) reported particularly on the mass of circulating blood which he found to be modified. He observed a progressive and proportional diminution of the plasma. There is also a reduction of the number of formed elements of the blood. Whereas the quantity of circulating red blood cells returned to normal, the oligocytosis persisted. The loss of plasma is produced when the blood traverses the burned region. These facts are of extreme importance, according to the author, in the early stage. He states finally that tannic acid is not antiseptic and this has led him to use certain modified solutions.

**L. Christophe** (Liège) interpreted the diminution of blood chlorides as due to an escape from the blood stream into the tissues.

**Dziembowski** (Bydgoszcz) reported on the treatment of burns by the local application of vitamins.

**R. Leriche** (Strasbourg) called attention to the use of sterile sheets. He considers tannic acid as the best treatment, but not in all cases, and since 1926 he has employed mercurochrome in infants and in burns about the face. Mercurochrome is especially recommended for infected burns.

**J. deFourmestraux** (Chartres) reported on burns of aviators. These patients die of bronchopneumonia or of pulmonary gangrene resulting from the gas due to the burning of gasoline. He reported a case in which he noted an absence of oliguria.

**Hamant** (Nancy) and **Grimant** (Algrange) reported on their interesting observations in which they resorted to the immediate excision of the burned region.

**Yves Bourde** and **Roger Gary** reported on 25 cases of burns which they studied. They called attention to some cases of burns in children who have presented a syndrome very similar to the syndrome of hyperpyrexia of nutrition. They advocated in these instances the use of cold applications. In the infected cases they resort to mercurochrome.

**P. Lombard** and **Montpellier** (Algeria) reported on the histologic findings of two interesting observations. In the first case a child of seven years of age having a burn occupying more than 50 per cent of the body surface died twenty-seven hours after the accident. Histologic examination disclosed only lesions of the tubules of the kidney. On the other hand, in the second case, which was a child of twelve years of age having a normal blood nitrogen, they noted a characteristic glomerulo-nephritis. They also noted degenerative lesions of the liver.

**Paul Piollet** and **H. Limousin** (Clermont-Ferrand) have employed vitamin A. which they believe diminishes the toxicity and favors cicatrization. In some cases they first applied mercurochrome and then compresses of cod liver oil.

**Yves-Delageniere** (Le Mans). These authors still employ alcohol dressings which was taught them by their former chief, Lecene, and which they employ under anesthesia of ethylene chloride. They call attention to the fact that the practicing physician, nurses, attendants, etc., should be instructed against the immediate application of oil or grease in cases of burns. The manuals of first aid should be corrected in this regard and advocate dry sterile dressings as the best immediate form of therapy before sending the patient to the surgical service.

**Chevallier** and **Carcassonne** (Marseilles) reported very favorable results with the use of vitamin A. They believe that it favors cicatrization and elasticity of the scar, which they believe is important, especially in the region of the articulations.

**J. Fiolle** and **T. Funck-Brentano**: **Arterial Emboli of the Extremities—Physiologic Pathology and Treatment.**

**J. Fiolle**: **The Physiological Pathology of the Arterial Emboli of the Extremities.**—After having rendered respect to the work of René Leriche, the author then discussed "lost" (manquée) emboli and "occult" emboli. The "lost" (manquée) emboli are those which, after having a sudden and dramatic onset, go on toward recovery without having provoked gangrene. The "occult" emboli are those which are not suggested by any signs indicative of embolus. These types are of interest, because they may indicate a possible mechanism of defense.

The author referred to the possible origin of emboli (thrombi originating from the heart or aneurysm, atheromatous plaques detached from an arterial wall). The author with his student, Haimovici, found that septic emboli play a most important rôle in coagulation. Whereas in 10 experimental aseptic emboli there was no important thrombosis except a clot of 2 or 3 cm., of 7 septic emboli in the dog there was extensive thrombosis extending towards the periphery from the point of obstruction.

The parietal lesion in the region of the embolus involves the intima (epithelial desquamation), very little of the media, but especially the adventitia (active endo-

thelial capillary reaction and considerable polynuclear infiltration). These lesions of arteritis are early and progressive and after the twelfth hour render embolectomy and suture of the arterial wall unlikely to be successful.

The most important factor in the pathologic physiology of emboli is the vasomotor reaction. Haimovici in his experimental investigations introduced into a vessel a small dilatable balloon which consisted of a segment of the jugular vein, having one extremity closed and the other extremity connected to a tube through which a variable quantity of fluid could be injected to inflate the balloon. He observed that there was no vasomotor reaction if the obliteration was incomplete, nor if the balloon was slowly dilated to produce complete obliteration. On the other hand, sudden complete distention produced a marked vasomotor reaction. These vasomotor reactions consisted of a spasm in the region of the obstruction in the artery. There is always spasm in the obliterated segment and in the distal branches of this segment in the arterioles and even the capillaries. This spasm could extend over to the collateral vessels and make itself manifest in the neighboring vessels even at a distance. The author calls this "arterial colic" and refers to the pain accompanying the vasoconstriction of the segment as such.

The pathway followed by the vasomotor reflexes passes by the way of the perivascular plexus which Leriche has pointed out and by the mixed nerves (Malmjeac and Haimovici). The origin of the reflex is perhaps in the endothelium, but it also may be in the adventitia. The author noted that some extensive thrombi could become enormous and completely out of proportion to the original embolus. The mechanism of this formation consists of lowering of the blood pressure distal to the embolus and stagnation of blood.

The collateral circulation may be formed by the long arterial anastomosis or by the numerous intermuscular branches. Following the occurrence of the embolus the collateral supply may be developed with some difficulty. The author calls attention to the fact that the dangerous zones are the bifurcations and in the zones where there is a juxtaposition of muscles with divergent insertions (Leriche).

The first period which follows the embolus is that of initial shock and is dominated by the vasomotor reaction (spasm). If the embolus is not too large or too infected, the spasm ceases. The collaterals enter into play and the embolus becomes a "lost" embolus. However, most cases enter into the second period, which consists of parietal alterations and extensive thrombosis. The deeper arterial lesion is followed by a periarteritis (Leriche). The third period is that of complications and is dangerous because cicatrization does not mean recovery.

#### P. Funck-Brentano: The Treatment of Arterial Emboli of the Extremities.—

Having recalled the work of Professor René Leriche, which is of prime importance in the rational treatment of emboli, the author divides the therapy into two groups. First, the anatomic method directed toward the embolus; second, the physiologic pathogenic method directed toward the sympathetics of the arteries. These two methods must not oppose each other, but they should be complementary.

The author first discussed the anatomic basis of the surgical treatment of arterial emboli. From experimental, clinical, and bacteriologic investigations it appears that in contact with the clot there is produced an endarteritis. The time of appearance of this endarteritis is variable. If the clot is large or septic, it appears early. This does not occur if the embolus is aseptic, if the obliteration is not complete, or if the collateral is immediately developed sufficiently. As a general rule, if the embolus is caused by a septic cardiac lesion, the time of appearance of the endarteritis is about ten hours.

The author next discussed the diagnosis of arterial emboli. There is marked pain which is very intense and localized in the involved area, but which may be diffuse and involve the entire extremity. This pain is due to the irritation of the

periarterial sympathetics by distention of the vessels (Leriche). The suddenness of the appearance of these signs is not constant and in a large proportion of cases the beginning is progressive. There is also pallor and coldness of the skin and a disappearance of skin sensitivity. The pulse is not perceptible and the reflexes are absent.

In the differential diagnosis phlebitis and arteritis must be considered. It should be recalled that phlebitis can produce the syndrome of arterial ischemia by an arterial spasm.

The differentiation between embolus and thrombosis of the artery by arteritis is also important (Einar Key). The presence of infection or intoxication is in favor of thrombosis. The presence of a cardiac lesion is in favor of embolus. In the case of embolus the oscillometer of Pachon shows an increased arterial pulsation above the obliteration and a diminution immediately below. On the other hand, in the case of thrombosis the diminution of oscillations is progressive. One can differentiate the embolus from arterial thrombus by the use of warm baths and by the use of vasodilators such as acetylcholine.

The diagnosis of the embolic attack is of very great importance. All of the authors are in accord in insisting on the frequency of the localization of the embolus at the points of bifurcation. Certain clinical observations such as the attack of pain, the thermal modifications, the signs of ischemia, and the pulse permit the localization of the embolus to a certain degree. But the most exact and useful method for the localization of the embolus is the arteriogram, which demonstrates precisely where one must intervene, indicates the number of emboli, and offers some information of the degree of collateral circulation.

In the absence of any therapeutic measures in cases of arterial emboli gangrene has been observed in 73 per cent of the cases if the subject is more than sixty years of age, and in 32 per cent of the cases if the subject is less than sixty years of age. There are some emboli that heal spontaneously. In other cases healing is incomplete, but usually gangrene develops.

As regards the therapeutic methods, the author begins by a discussion of the methods which attack the embolus. Embolectomy was successfully practiced for the first time in 1911 by the French surgeon, Georges Labey, but the Scandinavian surgeon, Einar Key, has been the leading pioneer of this form of therapy. This author published in 1923 the results of 36 embolectomies with 16 successful results. According to the present author the number of embolectomies published is 404. Of 108 observations published since July, 1932, the percentage of successful results on patients operated upon before the tenth hour was 70. The author discusses in detail the technique of embolectomy and insists upon the necessity of uncovering a large portion of the artery, of strict asepsis, and of employing an anticoagulant material (he prefers 2 per cent citrate solution).

The technique of embolectomy was discussed in considering the larger arterial trunks, such as the subclavian which can be exposed best in the hollow of the axilla, and the bifurcation of the aorta or the primary iliaes, which can be approached by the transperitoneal, retroperitoneal, or femoral route (Einar Key), and finally by the combined femoral and retroperitoneal routes.

Embolectomy is considered successful only if the permeability of the principal arterial trunk is reestablished. Absence of necrosis of the extremity is not sufficient. There must be reappearance of the arterial pulse. One of the arguments given by numerous authors against embolectomy is secondary thrombosis at the line of the suture. Actually, after embolectomy the thrombus is not the result of the method but the manner in which it is done. The thrombus is not the result of arteriotomy but of the preexisting endarteritis.

The mortality in general is sufficiently high. The author cites the work of Pearse which is based upon 296 embolectomies of which 52 per cent died less than a month after the operation. The late deaths are the result of the original lesion (chronic myocarditis, embolus, or cerebral hemorrhage, etc.).

A study of the results according to the age of the subject shows that an advanced age is not a contraindication to embolectomy and that a young age is not always a factor of good prognosis. As regards the arteries involved, the results are clearly better in interventions on the upper extremity than in those of the lower extremity, and in interventions on the superficial arteries than in those of the deeper arteries.

The time of the operation plays the principal rôle in the prognosis. The earlier the intervention after the occurrence of the embolus, the less is secondary thrombosis likely to occur. Reports on the statistics of the author (1932-1937) on 108 cases is in accord with the statistics of Key, of Pearse, and of Danzis. In those cases in which operation was performed within ten hours after the occurrence of the embolus, there were 70 per cent successful results. After the tenth hour on 26 cases there were only 6 good results.

The author concludes that if the procedure is applied in those cases in which it is definitely indicated embolectomy presents more advantages than disadvantages, and that in the future the successful results can be increased by the use of arteriography to localize precisely the site of the embolus and by adding a complementary procedure (sympathectomy or paravertebral novocaine infiltration of the sympathetics).

The author then discussed arteriectomy. This operation is based upon the knowledge of the physiopathology of the obliterated artery and the investigations of René Leriche. The procedure suppresses an irritative focus which obviates peripheral vasoconstriction.

The author discusses the technique of arteriectomy before and after embolectomy and concludes that it is preferable to do first ablation of the embolus and following this resection of the artery in the zone where the endothelium is involved.

In studying the indications for arteriectomy and for embolectomy, the author comes to the following conclusions: Before the tenth hour it is always necessary to do embolectomy; after the tenth hour arteriectomy is indicated. He advises exploratory arteriotomy in the late cases approaching the tenth hour. On the other hand, when it is later than this, he advocates arteriectomy without previously opening the artery. Furthermore, arteriectomy is indicated if the patient is very weak and incapable of withstanding a long intervention, such as embolectomy on one of the larger vessels, and if the embolectomy has failed in the instance where extirpation of the clot is impossible or where there is secondary thrombosis.

The intervention of the sympathetics consists of novocaine block or ablation of the communicating rami or the ganglia. For the lower extremities he advises the extirpation of the second, third, and fourth lumbar ganglia which gives the most intense vasodilatory action. For the upper extremity he advocates novocaine infiltration of the stellate ganglion, as described by Leriche.

Venous ligation has been advocated in the case of arterial obliteration by von Oppel who showed, in 1910, that it can produce an increase in the blood supply after ligation of the corresponding artery. In the light of the work which he discussed it is not considered an advisable procedure.

The author discussed in detail the pharmacodynamic treatment. He particularly studied the antispasmodic action of papaverine and the vasodilatory action of acetylcholine and of other sympathicolytic drugs (Yohimbine). He stated also that certain cardiac drugs are useful in relieving the peripheral circulation. But in general the medical treatment must simply be an aid to the surgical.

Finally the author discussed passive vascular exercise used particularly in the United States. The method has not escaped considerable criticism, and as yet the number of observations published limits its evaluation.

*Discussion.*—Jean Dedrna (Hradec Kralové) discussed the rôle of the lumbar sympathetics in the treatment of arterial embolectomy of the lower extremity.

F. Albert (Liège) stated that he always used infiltration of the lumbar sympathetics and vasodilatory drugs. As a result of his studies on the origin of peripheral vasoconstriction, he believes that venous ligation is indicated in certain types of cases.

Reynaldo dos Santos (Lisbon) discussed three points: (1) The importance of the extensiveness of spasm. He cited a case with endocarditis and gangrene of the nose and possible gangrene of the ears in which he noticed a marked cyanosis of the extremities which was suggestive of emboli of cardiac origin. Novocaine infiltration of the stellate on both sides immediately resulted in improvement. Later, autopsy confirmed the fact that there was no embolus and that the vascular disturbance was uniquely of spastic origin. In each type of case infiltration of the sympathetics with novocaine is extremely important. (2) Arteriography cannot show all of the arterial lesions. He has observed an extensive nodular syphilitic periarteritis which clinically had simulated embolus in a case in which the arteriogram was normal. Furthermore, by making two exposures with a slight interval between, each arteriography can show not only the proximal but also the distal limits of the obliterated artery. (3) As regards treatment he has a tendency to revert to the use of venous graft which he believes has the immediate advantage of counteracting the drop in pressure in the distal segment. He has been able to demonstrate persistence of circulation in the graft several months later by arteriographic examination. He believes that the graft is particularly indicated in the cases where the parietal lesion cannot be affected by simple embolectomy.

René Leriche (Strasbourg). Clinical observation, arteriography, and particularly the initial pain clearly indicate that much of the disturbance is due to the endothelial lesion, while some is due to the adventitia. On the basis of clinical investigations and in variance with the views of English and American authors, as well as Malmjæe and Haimovici, he contended that there exists a certain nervous conduction along the artery.

As regards the diagnosis, he believes that it is impossible to distinguish embolus from thrombus. The clinical signs and the suddenness of the symptoms are insufficient to establish embolus. Furthermore, he does not believe that arteriography can absolutely make the diagnosis. The most important diagnostic aid is to keep it constantly in mind. With the full realization of the frequency and importance of arterial spasm, Leriche cautions the surgeon not to make this diagnosis too eagerly, but to examine carefully for its presence.

As regards treatment he states that embolectomy aided by previous novocaine infiltration of the sympathetics is the ideal method. In the surgical treatment he states that it is important to visualize the artery. At one time he tried performing grafts after excision of the obliterated arterial segment. In his experience this has not been successful. But he believes that it is indicated today, because the patients are seen earlier, as dos Santos has noted.

Leriche believes that one can resect all of the arteries of the extremities except the aorta and the innominate. However, one should be careful in the resection of the bifurcation of the humoral artery and the origin of the tibio-peroneal trunk. The arteriectomies which give least clinical results are those of the smaller vessels.

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of Danis. It is about six and one-half months by plaster of Paris with the enclosed pin (technique of Böhler). Finally by the transosseous fixation (Creysse and Colson, and Merle D'Aubigné) it is four and one-half months; (3) the anatomic and functional results following these methods are: In the spiral fractures the classical orthopedic method (plaster of Paris) gives only 60 per cent good functional results. The modern orthopedic method (transcutaneous fixation) and the Lane plate method give very good results, 85 per cent for the bone plate, 80 per cent for the method of Böhler. In the transverse and oblique fractures the classic orthopedic method gives 66 per cent good results and the bone plate method 76 per cent good results. The authors note that the modern orthopedic methods do not give better results.

The authors then give the general indications. Transcutaneous fixation is advocated for recent spiral fractures. If there are counter-indications (a bad condition of the skin), continuous extension is employed. If the reduction is imperfect, especially if the fracture is seen two weeks after the accident, the wiring method of Danis, the screw fixation of Merle D'Aubigné, or the Kirschner method (Creysse) is best.

For transverse or oblique fractures, it is preferable to employ closed reduction and continuous extension in the plaster. If the reduction is impossible continuous extension or open reduction is necessary.

M. R. Danis (Bruxelles) stated that in order to reduce operative trauma and to induce good healing open fixation is considered as the method of choice and not as a last resort. Furthermore, it is necessary to avoid prolonged immobilization of the articulation above and below the fracture. For this reason he immobilizes the leg in a metal and cloth legging surrounded with celluloid which can be laced on so as to permit the knee and the ankle to be free. The bone fixation of the leg is made with a steel wire which is wound around the fragments. Spiral fractures are particularly adaptable to the wiring method and the results on 28 cases reported by the author treated by this method were excellent. In the transverse fractures the method is more difficult to employ and the results in 25 cases were considerably less favorable. In the latter types splinting by a graft of pure bone appeared to him to be a better method, because he has obtained excellent results in the cases in which he has employed it up to the present.

*Discussion.*—Lambotte (Anvers) discussed the open operative method.

Bouver (Namur) and Berburge (Anvers) prefer external fixation.

Jacobovici (Bucarest) described a ribbon encircling method with external fixation (Juvara), which easily permits the removal of the metal.

Leriche (Strasbourg) after having seen and employed various methods stated that he realizes more and more the advantages of metal fixation of the bone and prefers this method when an attempt at reduction has failed.

Stulz (Strasbourg) reported excellent results by open fixation on 30 cases in the clinic of Professor Leriche.

Chirolanza (Naples) preferred closed reduction.

Petre Topa (Bucarest) stated that he prefers the open method and fixes the bone by the simple graft of Jacoe which he removes on the fifteenth day.

Podlaha (Olomouc) stated that he prefers the orthopedic treatment and reserves the open fixation for the cases where this fails.

In spite of all treatment amputation is often necessary. But it is undeniable that operations on the arteries and sympathetics limit considerably the extent of the necessary sacrifices.

T. Wertheimer (Lyon) reported 3 interesting cases. He insisted upon the importance of arterial spasm and novocaine infiltration of the sympathetic chain.

Carcassone and Haimovici (Marseilles) related their interesting experience regarding the mechanical and vasomotor or spasmodic factors of the obliteration. They emphasized the importance of counteracting the spasm in the first stage by the use of vasodilator substances or novocaine infiltration of the sympathetics and arteriectomy for the arteritis in the second stage.

Marc Iselin (Paris) reported his observations on 4 recent cases and stressed the relative independence of function between the arterial trunk and the arterioles.

Naulleau insisted on the usefulness of arteriography and the therapeutic importance of the infiltration of the sympathetic chain. By graphic means he has proved that these infiltrations must be frequent and repeated.

R. Merle D'Aubigné and Jean Creyssel: *Relative Indications for Surgical Intervention and for Orthopedic Methods in Closed Fractures of the Leg.*—The authors reviewed the anatomic characteristics of fractures of the leg and distinguished two groups for diaphyseal fractures of the leg: transverse fractures and spiral fractures. The old group of oblique fractures should be classified under the first or second group according to their etiologic characteristics and radiologic findings.

The authors then discuss the anatomic results and the functional results. Is anatomic healing necessary to obtain a good functional result? The study of numerous statistics, including those of the authors, showed very well that there is a parallel between the anatomic state and the functional result. The following are the statistics of the authors on 219 observations: Of 68 perfect or very good anatomic results there are 67 perfect or very good functional results. In the other cases in which the anatomic results were poor, the functional results were also imperfect: 4.3 per cent if there was an overriding or overlapping of 2 cm.; 42 per cent if there was slight angulation; 80 per cent if the shortening was greater than 2 cm., even with a good axis. This shows the necessity for obtaining the best possible anatomic restitution.

The authors then discussed the best methods of treatment: (1) the classic orthopedic treatment; that is, manual reduction with application of plaster cast is insufficient because of the frequent secondary displacement, especially in spiral fractures; (2) the application of a Lane plate or wiring has the well-known disadvantage of infection and delayed healing; (3) the modern orthopedic method; that is, the classic orthopedic methods with various appliances: continuous transosseous extension (Putti, Kirschner); the fixation by transosseous wires included in the plaster cast (Böhler).

They then describe their personal method for spiral fractures, which consists of fixation by the double pin (Creyssel and Colson), and the pin method of Merle D'Aubigné. The authors, in comparing the results obtained by the various methods, note the following: (1) the risk of infection by Kirschner pin or by transcutaneous fixation is much less than by open reduction and metallic fixation; (2) the duration of the treatment according to the authors' observations is about five months by the old classic method if successful, but if it fails and it is necessary to employ some other technique the time increases to twelve months. It is about seven months by the Parham-Martin band method, but only four months by the wiring method

Dr. R. C. Sears, of the University of Oregon, described their system of examinations which is patterned after that of the University of Minnesota except that the committee is empowered to disregard failures and promote the student if it chooses to do so.

Dr. Robert P. Dobbie, of the University of Buffalo, presented a type of objective examination designed to eliminate inequalities in the grading of papers by so phrasing the questions that they are answerable by "yes" or "no" or by simple enumerations, yet extensive enough to serve as a real test of knowledge. Development and adoption of this type of examination was prompted by Dobbie's previous observation that, in correcting the essay type of examination, different examiners gave very different grades for the same answer; and the same examiner regrading the same paper after a considerable period without a record of the previous grade was very inconsistent.

With the new type of quiz, the average difference between examiners grading the same paper was one point: with the previous type it had been as high as 35 points.

Dr. E. Stanley Ryerson, of the University of Toronto, urged that more emphasis be placed in medical schools upon the recognition of the healthy state and upon its maintenance. Thus, courses in physical diagnosis of the normal person could well be begun, and closely integrated, with those in anatomy and physiology.

The second day was occupied by description of the organization of the curriculum at the Medical Schools of Leland Stanford and of the University of California. Reflected was the increasing tendency to introduce the student to clinical work early in his career, both schools starting it in the sophomore year.

Dr. George Barnett, of Stanford University, emphasized the value of sophomore clinics consisting at each session of a brief explanatory lecture followed by practical work with patients.

Dr. Frederick L. Reichert, of Stanford University, described the course in dog surgery given to sophomores. The main purpose of this course appears to be to teach the student early how to comport himself to the operating room so that he will not be a menace to the patient when he begins to help with operations on the human.

Dr. William Dock, also of Stanford University, took the position that the pathologist ought to concern himself with gross and microscopic pathology, leaving the clinical aspects largely to the clinicians.

Dr. Salvatore P. Lucia, of the University of California, discussed the organization of the senior curriculum at the University of California, emphasizing the use of the out-patient department which has been so organized that the student follows the patient into the hospital or into the home, as the case may be, thus securing a view of the patient which includes the social and economic as well as the clinical aspects of his situation. The object is to avoid a narrow view of the patient's ailment.

Dr. Frederick S. Bruckman, of the University of California, discussed further the importance of the out-patient clinic in teaching and especially emphasized the value of the time spent by the student with the social service workers, from whom he learns at first hand of the organization and function of the various welfare agencies and how to enlist their aid when necessary. An attempt is made to familiarize the student with the various items in the cost of medical care.

The third day began with a symposium on the community aspects of medicine. Dean H. R. Wahl, of the University of Kansas, attributed the new conditions

Auvray (Paris) having examined a number of cases noted that bad results of bone fixation methods are possible and that it must be employed with judgement by a qualified surgeon.

Fredet (Paris) preferred the open fixation method.

Judet (Paris) tries first the orthopedic method and if this fails he uses open fixation.

Dupuy de Frenner (Paris) uses the closed reduction method for cases seen early.

Others taking part in the discussion were Arnaud (Saint-Etienne), Lemaire (Courriere), Vanlande (Rabat), Marcel Senechel (Paris), Chevanez (Bordeaux), Pastalis (Paris), Delandeninert (Mons), Masmontille (Paris), Grinda (Nice), Serey (St. Malo), Rieneg (Toulouse), and Gentile (Nodent-sur-Marne).

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## REVIEW OF THE MEETING OF THE ASSOCIATION OF AMERICAN MEDICAL COLLEGES, SAN FRANCISCO, CALIF., OCT. 25-27, 1937

C. D. CREEVY, M.D., MINNEAPOLIS, MINN.

*(From the University Hospital)*

THE forty-eighth annual meeting of the Association of American Medical Colleges was held at the Fairmont Hotel, San Francisco, Calif., on October 25 to 27, 1937.

Dean E. W. MacEwen, of the Medical School of the University of Iowa, gave the first of four papers in a symposium on examinations. He pointed out that increases in the number of medical students have lessened individual contacts with instructors and enhanced the importance of the written examination. The fact that 25 per cent of the students admitted to our medical schools fail to finish suggests defects in the current system of examinations, but points also to inadequacies in selecting the students in the first place. The remedy for this high student mortality probably lies also in the selection of better teachers, bearing in mind that an excellent research worker may be a miserable teacher; and in improving the type of examination, perhaps by a shift to the objective form.

Dean H. S. Diehl, of the University of Minnesota, described the system of comprehensive examinations employed in the Medical School there for the past ten years. The questions are prepared by the various departments, reviewed by the examination committee for ambiguities and unfairness, and given annually, except in the fourth year, under the supervision of the chief examiner. Papers graded below passing are checked by a second examiner and, if still below grade, by the committee. The names of the students are not known to those correcting the papers. The student may repeat both the freshman and sophomore examinations once and may have three trials in the junior year. More failures than this lead to dismissal. The work of the next year may not be taken, in whole or in part, until the comprehensive examination of the preceding year has been passed.

Chief advantages of the system are its impartiality, the fact that the disturbances of students and faculty incident to examinations occur only once a year, and the necessity for reviewing the whole year's work as a unit. Moreover, the practice of rechecking the low papers insures fairness to the weak student. In the years 1935-1937, about 10 per cent of those taking the examinations were eliminated.

THE CENTENNIAL MEETING OF THE AMERICAN ASSOCIATION OF OBSTETRICIANS, GYNECOLOGISTS AND ABDOMINAL SURGEONS, HOT SPRINGS, VA.,  
SEPT. 20-22, 1937

JENNINGS C. LITZENBERG, M.D., MINNEAPOLIS, MINN.  
(From the University of Minnesota)

THE meeting of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, held at the Homestead Hotel, Hot Springs, Virginia, was the Centennial Celebration of the founding of the Society. It was held on September 20, 21, and 22.

**Improvements in the Operative Treatment of Carcinoma of the Large Bowel, W. Wayne Babcock, M.D., Philadelphia, Pa.:** Dr. Babcock called attention to the advantages of oblique muscle-splitting incision in resection of the large intestine for carcinoma. He discussed the prevention of peritonitis by preliminary decompression of the bowel, by vaccination of the peritoneum, and by semiasseptic methods of suture; the guarding of suture lines from peritoneal leakage by large glass tube drains; modifications of the Mikulicz operation with immediate drainage by external bulbous tubes; early division and suture of the spur with the aid of fine alloy steel wire sutures and ligatures; the removal of rectosigmoid growths by a modified abdominal Mikulicz procedure; the elimination of abdominal colostomy in rectal and sigmoid growths with establishment of a perineal anus, with or without preservation of the sphincters.

**Early Diagnosis of Carcinoma of the Fundus, J. P. Pratt, M.D., Detroit, Mich.:** Any vaginal bleeding after the menopause arouses suspicion of malignancy. Microscopic bleeding is important for early diagnosis. This is especially true when the cervix appears normal. Before the menopause, carcinoma occasionally originates in hyperplasia of the endometrium. All curettings must be examined carefully for evidence of malignancy. Dr. Pratt recommended that the patient be instructed to keep a graphic record of menstruation for three years. This sometimes leads to determination of early carcinoma. He also emphasized the necessity of careful education of patients as essential to secure earlier diagnosis.

**Three-Year End-Results of Carcinoma of the Female Genital Tract Treated with 800 K.V. Roentgen Rays, Henry Schmitz, M.D., Chicago, Ill.:** The effect of the Roentgen ray deep therapy is determined by histologic changes in the carcinoma cells. Sections were removed before treatment was begun and thereafter every eight days until the treatment was finished. These sections were studied every two weeks until local healing ensued. The radiation doses were 1,000, 2,000, 3,000, and 4,000 after one, two, three, and four weeks. The histologic changes due to the Roentgen rays of 800 K.V. were compared with those obtained with gamma rays. They were found to be essentially the same.

This treatment, from May 1, 1933, to December 1, 1934, showed a healing of 50 per cent in 34 patients.

Results after similar periods obtained with radium and 140 K.V. Roentgen rays were 20.8 per cent in 24 cases and with radium and 200 K.V. Roentgen rays were

Received for publication, December 27, 1937.

which confront the practitioner of medicine to changes in the social order brought about by the machine age, and especially to swift transportation and communication. He declared that prejudice against the medical practitioner, always fostered by the cultists, is often increased by the physician himself through insufficient participation in civic and community activities, apparent snobbishness, lack of sympathy, and excessive fees.

He urged that students be informed of the medical aspects of social security legislation already in effect, and made conscious of modern needs and facilities for the care of the indigent and near-indigent. He pointed out that, in the long run, society will choose for itself the type of medical care which it desires.

**Dr. B. W. Black**, of Alameda, Calif., entered a plea for unprejudiced presentation to the student of such widely divergent but controversial matters as contraception, euthanasia, health insurance, and state medicine. He declared that the present economic system is incompatible with the current code of medical ethics.

**Mr. Ralph Couch**, of the University of Oregon, pointed out that it is difficult if not impossible to teach a medical student to be ethical, since his tendency in this direction has probably become fairly well fixed by other factors and training prior to entering medical school. He is sure that socialization of medicine is on its way and urges that students be prepared for it by teaching all the details of medical economics, including bookkeeping, his responsibility to charity patients, the details of the income tax law, etc.

In the discussion, **Dr. Herman G. Weiskotten**, of Syracuse, N. Y., said that at Syracuse University they had approached the economic problem by requiring each student to make a complete social and economic study of one patient and to present the result at a seminar with the social service worker and the professors of medicine and psychiatry. They have also initiated a six weeks' clerkship in Public Health, during which the student not only visits but participates in the activities of the various public health and welfare agencies.

**Dr. Langley Porter**, Dean of the Medical School of the University of California, deplored the present-day tendency to forget that the medical student is an adult who has rights to some leisure for reflection after exposure to stimulating teachers. Students are usually better aware of practical economics than one might think and should be allowed to draw some conclusions of their own rather than to be too tightly crammed with facts in formal courses.

**Dr. Alan M. Chesney**, of Johns Hopkins University, said that Johns Hopkins employs a plan similar to that described by Dr. Weiskotten.

**Dr. Calvin P. Stone** and **Dr. George S. Johnson**, of Stanford University, presented the case for more adequate teaching of psychology to the premedical student and for its closer integration with subsequent studies of psychiatry by medical students. There was some deploring in connection with the small amount of time now devoted to psychology in the premedical curriculum and to psychiatry in the medical schools, leading the author to speculate idly upon the probable length of the medical curriculum if the pleas of each specialist for more emphasis and more time for his subject were heeded.

**Dean M. H. Rees**, of the School of Medicine of the University of Colorado, described Ebaugh's method of teaching psychobiology by means of personality studies of each freshman medical student, who is required to answer in detail an alarming array of questions (occupying twenty-four mimeographed sheets) concerning his past life and the intimate details of his behavior. While this must give the student an admirable insight into psychiatric methods, one cannot help but fear its effects upon the neurotic student with but little sense of humor.

**Respiration and Pulmonary Ventilation in Nonpregnant, Pregnant and Puerperal Women with an Interpretation of the Acid Base Balance During Normal Pregnancy, E. D. Plass, M.D., Iowa City, Ia.:** The respiratory rate, the volume of tidal air, and the minute volume of respired air increase during pregnancy. Associated with these changes there is an increase in the minute volumes of expired  $\text{CO}_2$  and of absorbed  $\text{O}_2$  and a rise in the ratio of the minute volume of respired air to the minute volume of expired carbon dioxide. The acid-base balance in the blood of pregnant women represents a compensated  $\text{CO}_2$  deficit based upon a physiologic hyperventilation, the gradual development of which prevents any consistent rise in the blood pH by permitting a reduction of the plasma bicarbonate proportional to the lowering of the  $\text{CO}_2$  content.

**What Is the Correct Interpretation of the Term Test of Labor? E. L. King, M.D., New Orleans, La.:** There is a lack of uniformity in the definitions of the "test of labor" which is found in the various textbooks on obstetrics. This term, of course, is applied to the conduct of labor in a case of borderline contracted pelvis. The question of the performance of Caesarean section is based upon the findings after the "test of labor."

**The Relationship of Fetal Birth Injuries to Obstetrical Difficulties, W. A. Scott, M.D., Toronto, Canada:** There is a tendency to ascribe fetal birth injuries to poor obstetrics. The practice of good obstetrics implies a certain fetal mortality and if attempts are made to eliminate this mortality, poor obstetrics will be done with an increasing maternal death rate.

This paper is a consideration of the factors in fetal birth injuries as encountered by conscientious obstetricians.

**Nutritional Diseases Associated with Late Toxemia, R. A. Ross, M.D., Durham, N. C.:** The apparent paradoxes in the incidence, causation, classification, treatment, and prognosis of patients with late toxemia of pregnancy have been repeatedly emphasized. Dr. Ross has been impressed with certain variances occurring in patients of North Carolina. His report comprises a five-year review of the problem of late toxemia of pregnancy in a state which is essentially rural, its incidence in a general hospital, and its development in an institution that has adequate professional supervision. The results are at variance with the findings of studies in other localities. He emphasized that the difference was probably due to the peculiarities in the diet of the poorer patients with which they have to deal.

The speaker of the evening at the banquet was **Francis P. Gaines**, President, Washington and Lee University, Lexington, Va. Dr. Gaines, a great orator and scholar, gave a scholarly and inspiring address on the **Overtones of Education**.



29.2 per cent in 48 cases. It is therefore probable that the use of ultrahigh voltage Roentgen rays will give superior percentages of good end-results or cures after a period of five years.

**Pelvic Tuberculosis, James E. King, M.D., Buffalo, N. Y.:** Dr. King reviewed 26 cases of pelvic tuberculosis, laying particular stress upon the postoperative sanatorium treatment.

**The Surgical Treatment of Ovarian Dysfunctions, J. L. Reycraft, M.D., Cleveland, Ohio:** Different types of surgical treatment were reviewed and a series of cases presented, showing the functional effect of excision of the major portion of the ovarian cortex.

**The Problem of Endometriosis, Dr. Daniel Dougal, Manchester 3, England:** Dr. Dougal was the guest speaker at the meeting and delivered the Joseph Price Oration.

**Caesarean Section in Infected Cases, Willard R. Cooke, M.D., Galveston, Tex.:** Dr. Cook called attention to the unsatisfactory results of the Kroenig, Latzko, Hirst, Porro, Portes operations and proposed a modification of the Hirst principle, namely the isolation of the pelvic cavity by uniting the peritoneum of the uterus with the parietal peritoneum.

**Frank-Geist Operation for Congenital Absence of the Vagina, Walter T. Dannreuther, M.D., New York, N. Y.:** Dr. Dannreuther reviewed the various methods of constructing the vaginal canal, stressing the unsatisfactory results in most of them. The Frank-Geist operation has been popularized as the "satchel handle" operation, which is characterized by the construction of a canal of the skin and integument of the thigh and the dissection of a space anterior to the rectum into which the "satchel handle" is introduced.

**The Treatment of Vesicovaginal Fistula, Cameron Duncan, M.D., Brooklyn, N. Y.:** Dr. Duncan emphasized the necessity of cystoscopic examination, the determination of the function of the kidneys, the exact relation of the ureters to the fistula as necessary preliminaries to the operation.

**Gynoplastic Repair, Following Delivery, Raymond C. King, M.D., Toledo, Ohio:** Dr. King advocated routine examination of the cervix and vagina immediately following delivery. He stated that the immediate repair of recent injuries was superior to the intermediate repair (five to ten days after delivery). He called attention to the fact that intermediate or secondary repairs can be done immediately after delivery, but that it is wiser to postpone such operations to a later date.

**Presidential Address (Our Association, Its Privileges, Accomplishments and Its Future), James W. Kennedy, M.D., Philadelphia, Pa.:** This was a most inspiring review of the past history and future of the specialty of obstetrics and gynecology, paying high tribute to Dr. Kennedy's former chief, Dr. Joseph Price.

**The Preliminary Stage of Labor, Buford G. Hamilton, M.D., Kansas City, Mo.:** By the preliminary period of labor is designated all the presumptive signs of labor that may be present before there is evidence of the progressive softening, effacement, and dilatation of the cervix. Dr. Hamilton classified labor under three headings: true labor, false labor, or preliminary labor. In the latter there may be pains for days, with no progress, but the delivery is normal with proper handling. He stressed that during this period of prolonged ineffective pains interference is contraindicated.

that illustrate principles but not details. The literature of the subject has not been fully covered but perhaps that is not necessary in a work of this limited scope. The analysis of the 155 cases is of great interest in showing conditions faced by our French colleagues and especially in showing how they meet these problems. The operability for cure is 50 per cent, about that in many clinics in this country. The operative mortality and end-results in the various types of surgical attack are carefully analyzed and will be read with profit by anyone doing this type of surgery.

The first part of the monograph could be read with profit by the medical student; the second part, studied with interest by the surgeon as a comparison between his work and that of French surgery. It is worthy of note that at the present rate of exchange this book costs just over \$1.00. This low price is accounted for in part by the simplicity of the cuts and the paper binding, but we may well inquire whether there might not be a place in our literature for inexpensive books of this type in which subjects are covered comprehensively enough for the medical student, interne, and young surgeon. Surgery advances with such rapidity that the most expensive book soon becomes obsolete.

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**Tumors of the Nervous System** (Volume XVI of a series of research publications, The Proceedings of the Association for Research in Nervous and Mental Diseases, New York, Dec. 27 and 28, 1935). Pp. 493, with 213 illustrations, Baltimore, 1937, The Williams & Wilkins Co. \$7.50.

This book is a most excellent compilation of some of the recent advances in the investigation of tumors of the nervous system. It is composed of a series of individual articles written by investigators well versed in their particular fields. The subject matter comprising this book was presented at the annual meeting of the Association for Research of Nervous and Mental Diseases. Discussions of the papers are included after each chapter. These discussions help to elucidate the differences of opinion upon various subjects and are a valuable adjunct to the book.

As a whole, the articles are well written and concise. Certain chapters merit special comment. The chapter on "The Effect of Irradiation on Gliomas" is the result of a survey of material obtained by the pooling of cases from numerous clinics. This cooperative study has resulted in information which probably would be very difficult to duplicate. The study on "The Gliomas of the Central Nervous System" is an exceptionally well-written comprehensive review of the histologic structure of these various tumors and of the preoperative duration of symptoms as well as the average survival time in the various types of gliomas. The study of meningiomas has been approached from a new angle, and an attempt has been made to trace the origin of these tumors in order to account for the extreme variation in their structure. In this work the author very logically classifies the meningiomas according to their origin, thus emulating a procedure that already has been carried out for the gliomas. The final chapters are devoted to a study of "Tumors of the Peripheral Nerves." The authors here have succeeded in condensing and clarifying a most diversified and complicated field into a few well-organized chapters.

This publication, however, has certain definite weaknesses. The space allotted for the discussion of some of the subjects is certainly not in the proper proportion to their relative importance, thus producing an improper balance of the subject matter of the text. For example, an entire chapter is devoted to the study of "Ependymomas"—incidentally, an excellent chapter that warrants reading—while

## Book Reviews

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**A Brief Outline of Modern Treatment of Fractures.** Ed. 2. By H. Waldo Spiers. Pp. 133, with 109 illustrations and 5 plates. Baltimore, 1937, William Wood & Company. \$2.

In this small book the author has attempted the extremely difficult feat of compressing the subject matter of fracture treatment within the limits of the students' time and needs. The plan and general arrangement of the book are excellent and good use has been made of line drawings to illustrate the text. All padding in the form of reviews of the literature and extended discussion and debate has been rigorously excluded.

As a supplement to the teaching of students, however, the book is open to some few criticisms. The author has compressed his subject matter into the smallest possible compass, but he has not well adapted his style to the limits of his space. By careful editing and repeating polishing much space which is sorely needed for expansion and elaboration of certain parts could be gained.

The chapters on the treatment of individual fractures are, on the whole, good. Fractures of the clavicle are discussed in the traditional manner but without mention of Boehler's ideas on the subject. Dislocation of the shoulder joint is briefly and not too well considered, and unfortunately the original method of reduction as presented by Kocher is not accurately described. Fractures of the humerus are well treated, as are the fractures of the elbow joint. Colles fracture is considered in the orthodox manner, but no mention is made of Boehler's treatment. Fractures of the hand and carpal bone receive adequate mention for a book of this type. Fractures of the vertebrae and ribs are well described and discussed. The chapters on fractures of the hip and femoral shaft are remarkably good and compare favorably with those in any of the large texts.

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**Traitement Chirurgical du Cancer du Colon Pelvien.** By Pierre Bertrand and E. Corajod. Paper. Pp. 207, with 35 illustrations. Paris, 1936, Masson and Cie. 30 fr.

This book is one of the monographs on sharply delimited subjects so popular with the French and so well done by them. The authors are the former and the present Chef de Clinique Chirurgicale à la Faculté de Médecine de Lyon, also assistants to Professor Tixier of that clinic. The work is a critical analysis of 155 patients with cancer of the sigmoid colon treated in the surgical clinics of Professor Tixier and Doctor Paul Santy. The book is divided into two parts, the first dealing with the anatomy, pathology and clinical manifestations and the diagnosis of the part and the disease. These subjects are covered systematically but with brevity and without evidence of originality or personal authority. The second and larger part of the book is devoted to a consideration of treatment.

The historical development of the operative procedures is well done and most interesting, showing that American surgical literature has not given credit to the French for originating many commonly used technical procedures. All operations with their many minor modifications that have been used in treating cancer of the sigmoid are described briefly and illustrated with rather schematic line drawings

that illustrate principles but not details. The literature of the subject has not been fully covered but perhaps that is not necessary in a work of this limited scope. The analysis of the 155 cases is of great interest in showing conditions faced by our French colleagues and especially in showing how they meet these problems. The operability for cure is 50 per cent, about that in many clinics in this country. The operative mortality and end-results in the various types of surgical attack are carefully analyzed and will be read with profit by anyone doing this type of surgery.

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such tumors as pinenomas, oligodendrogliomas, and spongioblastoma polare are dismissed with only a very short discussion. Also, some forty-eight pages are devoted to a discussion of tumors and cysts of the cerebellopontine angle and their relation to the lateral recesses of the fourth ventricle. Such a lengthy discourse is somewhat out of keeping with the importance of this material to the rest of the book. The text is likewise lacking in completeness as a study of tumors of the central nervous system. The entire group of vascular tumors is omitted. Also numerous other less common lesions, such as teratomas, lipomas, and granulomatous lesions as tuberculomas and syphilomas, are not mentioned.

For the material covered, the book certainly can be recommended as an authoritative and well-written statement, but it cannot be used as a reference book for all tumors of the nervous system.

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**A Synopsis of Genito-Urinary Diseases.** By Austin I. Dodson. Pp. 272, with 111 illustrations, St. Louis, 1937, The C. V. Mosby Company. \$3.

This little book is designed to furnish the medical student and general practitioner with a convenient hand book of urologic information. This is the second edition, the first having appeared in 1934. The newer work is considerably improved over the original, both in the arrangement and treatment of subject matter and in the number of illustrations.

The outstanding feature of the book is its compactness and adherence to fundamentals. The author apparently realized the importance of describing in detail the points of technique in the performance of the simplest urologic procedures, since the book will be used for the most part by men entirely unfamiliar with urology. This alone makes it a valuable reference work, as these points are commonly slurred over or omitted in the larger, standard texts. The more advanced aspects of treatment, notably major urologic surgery, are passed over with the barest mention, as these are admittedly not within the scope of such a synopsis. Attention is paid throughout to the more common urologic conditions, the rarer diseases being mentioned but not emphasized.

The author has brought his book up to date and has included all of the newer urinary antiseptics in his discussion of upper tract infections. In addition to this, complete diet lists are furnished, which can easily be referred to in prescribing for patients. However, no misleading claims or inferences are made wherever new methods of treatment are discussed, and it is clearly stated in each instance that their efficacy and safety have yet to be tested by sufficient time and experience.

It may be seen from the above that this little book fulfills its purpose admirably and can unhesitatingly be recommended as a ready source of urologic information to any one desiring it.

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# SURGERY

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## Editorial Communications

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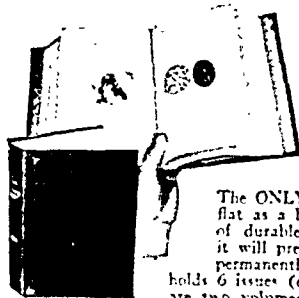
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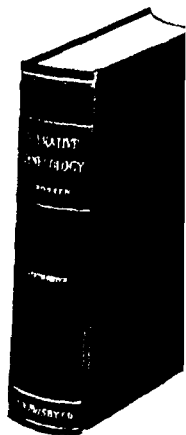
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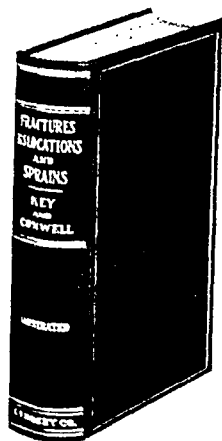
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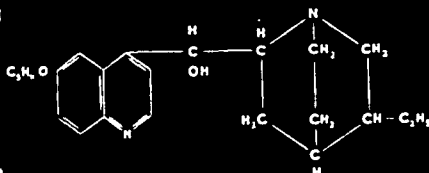
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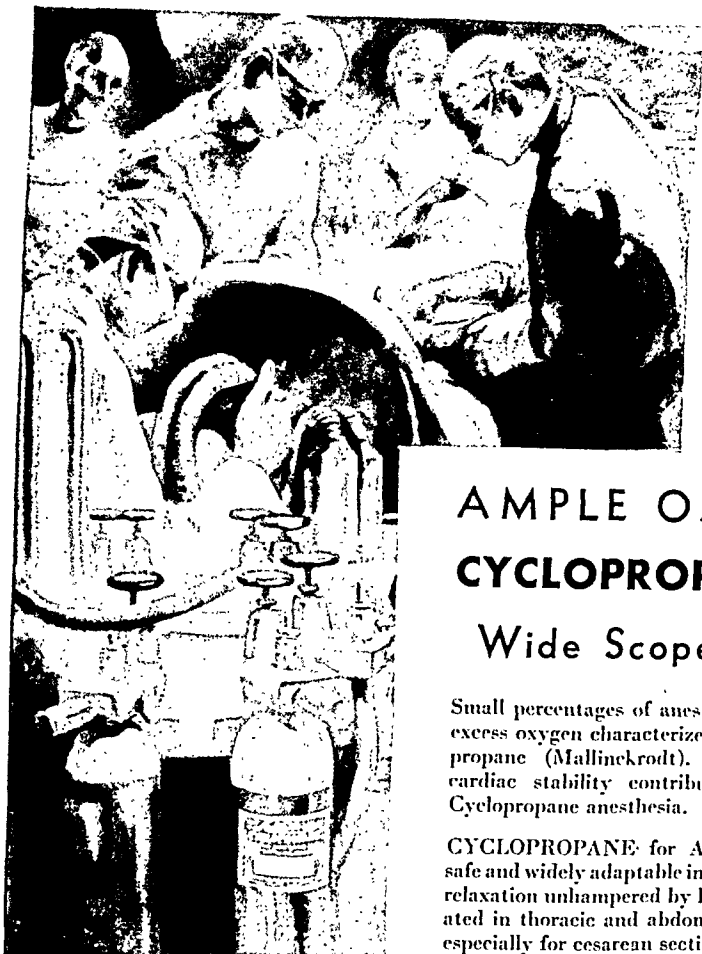


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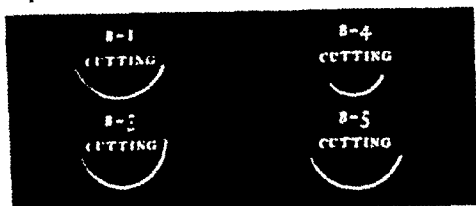
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1663...	Plain Catgut	4-0	B-5
1665...	Black Silk	6-0	B-1
1665...	Black Silk	4-0	B-1
1667...	Plain Catgut	5-0	B-4
1669...	10-Day Catgut	4-0	B-5
1669...	10-Day Catgut	3-0	B-5
1669b...	10-Day Catgut †	4-0	B-5
1669b...	10-Day Catgut †	3-0	B-5

### DOUBLE ARMED

1662...	Black Silk *	6-0	B-3
1664...	Black Silk *	6-0	B-1
1664...	Black Silk *	4-0	B-1
1666...	Plain Catgut *	3-0	B-4
1668...	10-Day Catgut *	4-0	B-5
1668...	10-Day Catgut *	3-0	B-5
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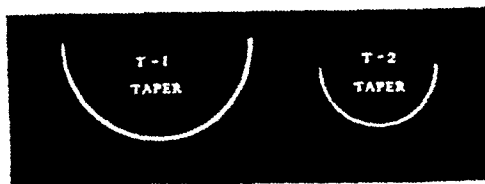
NO.	MATERIAL	SIZE	NEEDLE
1751...	Kal-dermic	8-0	C-1
1752...	Aluminum-Bronze Wire	00	C-1
1753...	Black Braided Silk	000	C-2
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NO.	MATERIAL	SIZE	NEEDLE
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1625...	Boilable Plain Catgut	0	T-1
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1651...	Kal-dermic	8-0	B-1
1651...	Kal-dermic	6-0	B-1
1652...	Kal-dermic	8-0	B-5
1652...	Kal-dermic	6-0	B-5
1652...	Kal-dermic	4-0	B-5
1653...	Black Silk-worm	4-0	B-1
1655...	Kal-dermic	4-0	B-2
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1504...Small $\frac{1}{2}$ -Circle Needle...A-4.....		4.20
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1541...Straight Needle.....	A-1.....	\$3.60
1542...Two Straight Needles....	A-1.....	4.20
1543... $\frac{3}{8}$ -Circle Needle.....	A-3.....	4.20
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1304...Small $\frac{1}{2}$ -Circle Needle...A-4.....		4.20
1305... $\frac{1}{2}$ -Circle Needle.....	A-5.....	4.20

### 20-Day Chromic Catgut:

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1342...Two Straight Needles....	A-1.....	4.20
1343... $\frac{3}{8}$ -Circle Needle.....	A-3.....	4.20
1344...Small $\frac{1}{2}$ -Circle Needle...A-4.....		4.20
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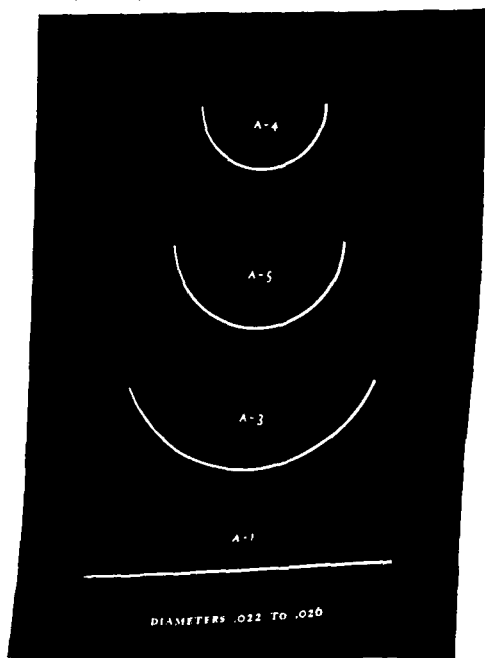
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1352...Two Straight Needles*..A-1.....		4.20
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1374...Small $\frac{1}{2}$ -Circle Needle*..A-4.....		4.20

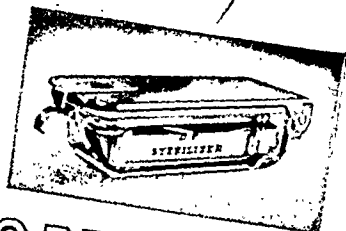
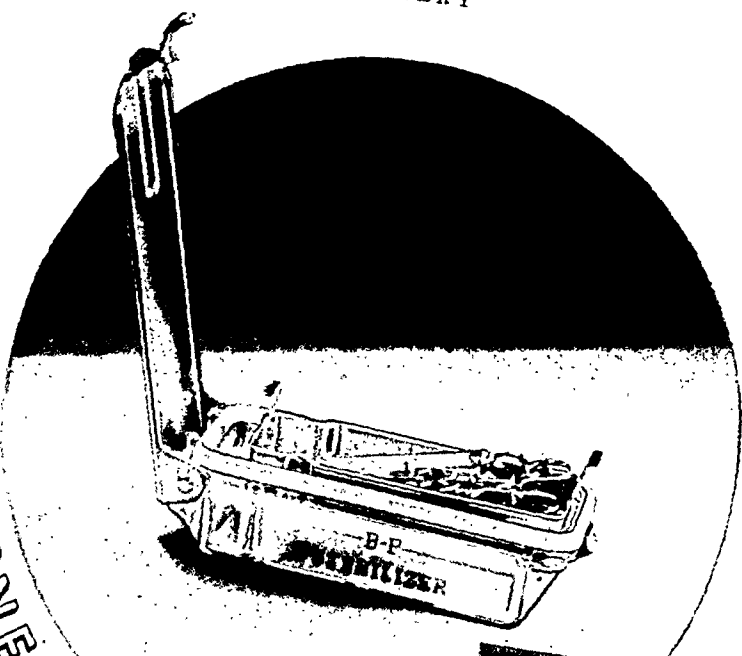
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## CONTENTS FOR MARCH, 1938

## Original Communications

- Effect of the Volatile Base in Fluid Intestinal Contents on Dogs With Low Intestinal Obstruction.* James S. Hibbard, M.D., M.S. in Surgery, Wichita, Kan., and Arnold J. Kremen, M.B., B.S., Minneapolis, Minn. 325
- Acute Intestinal Obstruction. I. The Role of Bacteria in Closed Jejunal Loops.* Sarah Haerem, B.S., G. M. Duck, M.D., Ph.D., and Harwell Wilson, M.D., Chicago, Ill. 333
- Acute Intestinal Obstruction. II. The Permeability of Obstructed Bowel Segments of Dogs to "Clostridium botulinum" Toxin.* Sarah Haerem, B.S., G. M. Duck, M.D., Ph.D., and Lester P. Dragstedt, M.D., Ph.D., Chicago, Ill. 339
- Pneumoperitoneum in Perforations of the Gastrointestinal Tract.* J. Randolph Palne, M.D., and Leo G. Rigler, M.D., Minneapolis, Minn. 351
- Peptic Ulcers Following Experimentally Produced Obstructive Jaundice.* Warren H. Hebert, M.D., Rochester, Minn. 370
- Diffuse, Cavernous Hemangioma of the Rectum.* Louis A. Buie, M.D., and Jerrold P. Nesselrodt, M.D., Rochester, Minn. 379
- Subphrenic Abscess.* L. J. Gogol, M.D., Los Angeles, Calif. 386
- Urethral Urinary Extravasation.* Nelse F. Ockerblad, M.D., and Hjalmar E. Carlson, M.D., Kansas City 391
- Concerning Renal Function and Structure Following Trauma of the Kidney.* John H. Powers, M.D., Cooperstown, N. Y. 397
- Newer Concepts in the Treatment of Injuries to the Ligaments of the Knee Joint: an Evaluation of the Mauck Operation.* M. Thomas Horwitz, M.D., and Arthur J. Davidson, M.D., Philadelphia, Pa. 407
- Posterior Dislocation of the First Cervical Vertebra With Fracture of the Odontoid Process.* Rudolph S. Reich, M.D., Cleveland, Ohio 416
- Rectovaginal Cloaca.* Charles W. Mayo, M.D., and Winfield L. Butsch, M.D., Rochester, Minn. 421

## Editorials

- Opportunities for Graduate Training in Surgery.* Elliott C. Cutler, M.D., Boston, Mass. 424
- Is Judgment Necessarily Inarticulate?* Edwin P. Lehman, M.D., University, Va. 427

## Recent Advances in Surgery

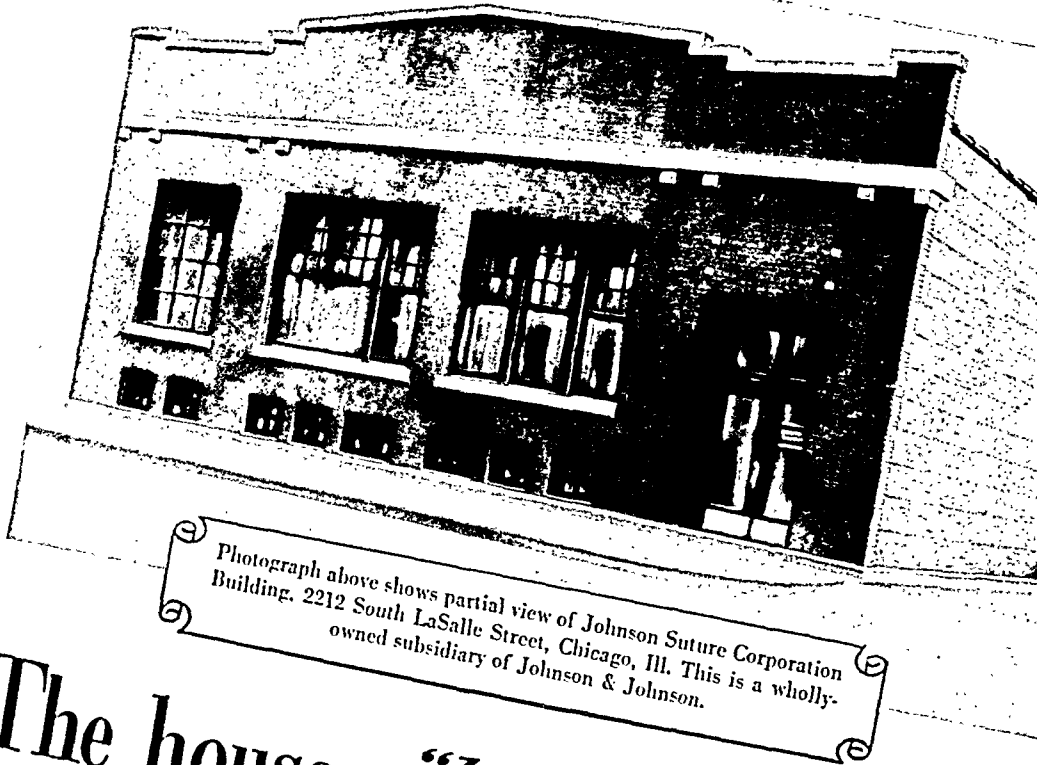
- Recent Advances in the Study of Burns.* Henry N. Harkins, M.D., Ph.D., Chicago, Ill. 430

## Review of Recent Meetings

- Report of the Forty-Seventh Annual Meeting of the Western Surgical Association, Indianapolis, Ind., Dec. 3 and 4, 1937.* Warren H. Cole, M.D., Chicago, Ill. 460
- Review of the Southern Surgical Association Meeting, Dec. 7-9, 1937, Birmingham, Ala.* Howard R. Mahorner, M.D., New Orleans, La. 470

## Book Reviews

- Book Reviews* 479



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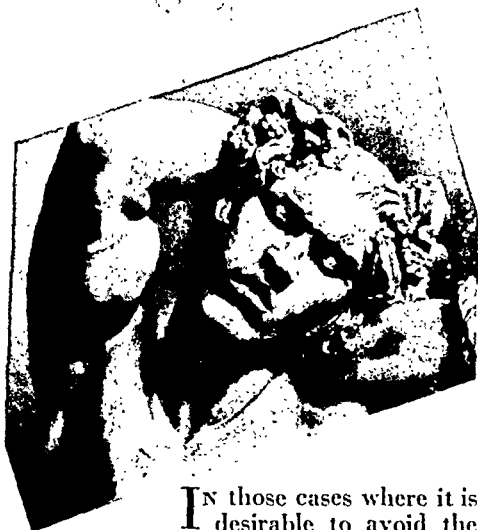
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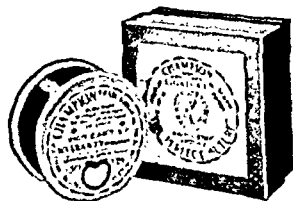
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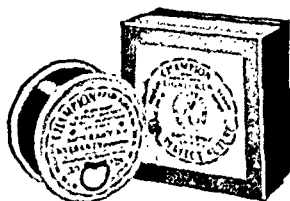
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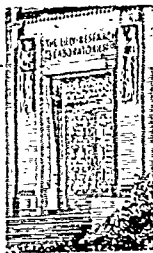
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# SURGERY

VOL. 3

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No. 3

## Original Communications

### EFFECT OF THE VOLATILE BASE IN FLUID INTESTINAL CONTENTS ON DOGS WITH LOW INTESTINAL OBSTRUCTION

JAMES S. HIBBARD, M.D., M.S. IN SURGERY, WICHITA, KAN., AND  
ARNOLD J. KREMEN, M.B., B.S., MINNEAPOLIS, MINN.

*(From the Department of Surgery, University of Minnesota)*

IN THE literature theories as to the cause of the symptoms and death in cases of mechanical obstruction are numerous. Some writers have accepted the dictum that a toxic substance was present in the intestine. As a result there have been thorough investigations of the fluid contents of the bowel to ascertain the existence of such toxins.

In a previous study one of the authors (J. S. H.)<sup>5</sup> showed that the gases occurring in low ileal obstruction could not cause symptoms of toxicity, provided their percentage was not greater than that found in simple obstruction.

The appearance of the volatile basic group of gases was entirely unexpected, since they had not been previously reported. Although this group of gases was harmless, added information consisting of an investigation of the volatile bases of the fluid contents, since they were in all probability the direct precursors of the gases, appeared to be important.

#### EXPERIMENTAL MATERIAL AND METHODS

The fluid contents of the obstructed intestines were collected immediately following death of the animal for analysis.

The total amount of volatile basic substance was determined by using a known amount of fresh contents from obstructed bowels and diluting with 200 c.c. of distilled water. To this was added 2 gm. of magnesium oxide to make the solution alkaline. The distillate from this mixture was trapped in a known amount of standard acid (one-tenth normal  $H_2SO_4$ ), which was then titrated with a standard base (one-tenth normal NaOH), using methyl orange as an indicator. The decrease in acid is equivalent

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to the amount of volatile base in the intestinal contents. In our study the percentage of volatile base is calculated on the basis of ammonia equivalent to the decrease of standard acid, although actually this is only about 50 per cent ammonia.

The ammonia was determined by thoroughly mixing the distillate with Permutit, decanting the supernatant solution, and washing the Permutit with distilled water. Alkalized water (NaOH) was then added to release the ammonia, the solution was Nesslerized and compared colorimetrically with a standard ammonia solution similarly Nesslerized. Qualitative tests for primary, secondary, and tertiary amines were made on the ammonia free portion by the method described by Hinburg.<sup>11</sup>

Hydrogen ion concentrations were determined with a Leeds-Northrup quinhydrone electrode.

Distillates for injection into normal dogs were made by adding magnesium oxide to intestinal contents of obstructed dogs and employing steam distillation. In this way the necessity of trapping the distillate, as was described above in the analysis of the contents, was obviated.

The volatile base which developed in the fluid contents of the small bowel was investigated by four types of experiments.

In Group A simple mechanical obstruction was produced in 8 dogs by dividing the intestine at the ileocecal junction and inverting the ends. The animals were given a mixed diet before and after the operation. At intervals of from three to nine days they were killed and the intestinal fluid was removed for study.

TABLE I  
GROUP A.—SIMPLE ILEAL OBSTRUCTION

ANIMAL NO.	WEIGHT POUNDS	FLUID CONTENT OF BOWEL CONTENT	VOLATILE BASE PER-CENTAGE	pH	DURATION OF EXPERIMENT DAYS	CONDITION OF ANIMAL
22	55	1198	0.416	-	3	Good
24	26	580	0.34	-	9	Fair
32	32	-	1.23	-	6	Dead
34	34	200	1.60	-	7	Good
35	36	400	1.45	-	5	Poor
36	32	750	1.61	7.3	6	Good
101	35	-	1.30	7.8	5	Poor
42	42	-	0.14	7.5	5	Good

In Group B long closed loop (127 to 178 cm.) obstructions were studied in 4 dogs. The obstruction was done in two stages, first leaving the distal end of the loop open as a blind enterostomy; and at the second stage 50 to 100 c.c. of intestinal contents taken from an ileostomy, performed on a normal dog, were injected into the loop, after which the obstruction was completed.

TABLE II

GROUP B.—CLOSED LOOP OBSTRUCTION OF SMALL INTESTINE

ANIMAL NO.	WEIGHT POUNDS	FLUID CONTENT OF BOWEL CONTENT	VOLATILE BASE PER-CENTAGE	pH	DURATION OF EXPERIMENT DAYS	CONDITION OF ANIMAL
19	55	225	0.38	-	3	Good
27	37	-	1.0	-	2.8	Dead
28	55	130	0.378	-	6	Poor
38	42	1050	0.254	-	3	Good

## EFFECTS OF A PROTEIN DIET

Many writers are of the opinion that a diet consisting only of meat causes early death in intestinal obstruction. On account of this belief, Group C dogs (7) were given a pure meat diet before operation and 2 dogs were given a relatively meat-free diet. They were autopsied immediately following death and the fluid contents were analyzed.

TABLE III

GROUP C.—EFFECTS OF PROTEIN DIET ON SIMPLE ILEAL OBSTRUCTION

ANIMAL NO.	WEIGHT POUNDS	DURATION OF LIFE DAYS	DIET*	FLUID CONTENT OF BOWEL CONTENT	VOLATILE BASE PER-CENTAGE	NH <sub>3</sub> PER-CENTAGE	pH
118	44	3	Meat	200	0.43	0.212	7.9
119	55	3	Meat	400	0.476	0.288	-
122	52	3	Meat	-	-	-	7.8
123	36	1.25	Meat	250	0.43	0.24	-
124	50	2.5	Meat	700	0.325	0.18	7.6
126	56	3	Meat	700	0.36	-	-
110	48	3.75	Meat post-operatively	300	0.519	-	-
121	56	5	No meat	700	0.2	0.11	-
117	44	24	No meat	1700	0.082	0.044	-

\*Diet was given for three days previous to operation and continued until death of the experimental animal.

## TOXIC EFFECTS OF THE VOLATILE BASES

Since some authors uphold the toxic theory, it was thought advisable to test the toxicity of the distillate containing the volatile bases, as compared to the volatile base free residue (Table V). The alkalinity of the distillate was so high that it was necessary to lower it, by the addition of hydrochloric acid, to about a pH of 8 which is the level occurring at death in simple mechanical obstruction. In 3 dogs the standardized distillate was injected into long closed loops extending from the duodenum to the ileum. In order to obviate the tension factor in the loop, 3 dogs which had esophogostomies with closure of the distal end were obstructed at the ileocecal junction and the distillate was injected into the closed intestinal loop without force. In Dog 138 a large amount of distillate was continually irrigated through the small intestine, being inserted through a duodenal tube and collected by an ileal tube.

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## INFLUENCE OF PROTEIN DIET

Since Whipple<sup>12</sup> and his coworkers have demonstrated that there is an increased destruction of protein in intestinal obstruction, a preponderance of volatile bases would be expected to occur in animals fed on a meat diet. However, these experiments (Group C) show the concentration to be only slightly greater than that observed in dogs receiving an ordinary diet (Groups A and B), although much greater than in two animals fed a relatively protein-free diet (Nos. 121, 117).

In this group the fluid contents were further analyzed for ammonia, primary, secondary, and tertiary amines as previously described. The results showed that the percentage of ammonia consistently amounted to about one-half of the volatile basic group. The remaining one-half gave positive qualitative tests for primary and tertiary, but negative reactions for secondary amines.

One of the important deductions to be derived from this group is that the animals not only showed earlier signs of toxicity, but that their length of life was greatly shortened. The average was three days as compared to seven days in dogs fed ordinary diets. One dog receiving a relatively meat-free diet lived twenty-four days.

It appears, therefore, that the end-products of protein putrefaction, if not primarily responsible for the cause of death in low ileal obstruction, certainly accelerate a fatal outcome. If the former instance were true, it may be concluded that when the percentage of volatile bases reached a certain fixed concentration, death occurred. Moreover, the high percentage of volatile bases found after death or when the fluid contents were allowed to stand, showed that the chemical action did not stop when it reached the antemortem level. But inasmuch as some of the dogs, with average volatile base levels, were in excellent condition when sacrificed, some other factor must serve in combination with the volatile bases.

## SIGNIFICANCE OF THE H-ION CONCENTRATION OF THE FLUID CONTENTS

It has previously been shown<sup>5</sup> that, in contrast to the acid reaction of normal intestinal contents as described by McCleendon, Shedlow, and Karpman,<sup>10</sup> Thompson,<sup>9</sup> Grayzel and Miller,<sup>4</sup> Graham and Emery,<sup>3</sup> the contents of the obstructed intestine were alkaline. It was also demonstrated that the alkalinity of the fluid contents increased in proportion to the duration of the obstruction until it reached its maximum, a pH of about 8, just before death occurred. After death or if the contents were allowed to stand, the pH decreased rapidly to the acid side.

Wilkie<sup>11</sup> has injected the intestinal contents, obtained from dogs with obstruction, into the bowel of a normal dog without ill effects. Also others<sup>1</sup> have demonstrated that toxic symptoms do not develop when the contents obtained from animals with intestinal obstruction were placed in the bowel of normal animals. The outcome would have been different

## TOXICITY OF THE BASIC RESIDUE

In order to compare the residue with the distillate, the following experiments were done. The residue was prepared by heating the intestinal contents of dogs dying from intestinal obstruction to 100° F. and by then distilling it by partial vacuum. The pH of the residue was standardized so as to give a similar reading as is found in intestinal obstruction at death. In 2 dogs the residue was injected into a closed loop extending from the duodenum to the ileum, and in 2 dogs the closed loop extended from the esophagus to the ileocecal junction.

## COMMENTS AND RESULTS

It is generally conceded that ammonia, amines, etc., produced in the intestine are products of protein putrefaction. Mathews<sup>7</sup> and Macleod<sup>8</sup> showed that ammonia is split from the protein during digestion and absorption. A part arose from the acid amide as a result of the putrefactive action of bacteria. Still another part was produced by the partial deamination of the amino-acids during the process of absorption. In addition Mathews pointed out that a large amount of ammonia occurred in the pancreatic secretions as well as in the gastric and intestinal mucosa (40 mg. per 100 gm. of fluid and 36 mg. per 100 gm. of tissue respectively). In all probability the volatile bases as a group originate in this manner.

Cholopoff<sup>2</sup> showed that normal arterial blood contains 0.01 to 0.02 mg. of ammonia per 100 c.c. of blood. In its passage through the wall of the large intestine and also at times through the wall of the small intestine, the blood absorbs ammonia, more with a meat diet and less with a carbohydrate diet, so that the ammonia content in the portal vein after a meat diet may rise to 0.06 mg. per 100 c.c. In the liver a good part of this absorbed ammonia is removed, the hepatic vein showing less ammonia than the portal vein.\*

## QUANTITATIVE DETERMINATION OF THE VOLATILE BASES

The results given in Table I, Group A, show that the volatile bases occurred in the fluid contents in association with low ileal obstruction, in amounts varying from 0.14 per cent to 1.60 per cent. There appeared to be no relationship between the duration of the obstruction and the concentration of the volatile bases. Likewise the concentration of the volatile bases per se had little influence on the condition of the experimental animal. Similar results were observed in the long closed loop obstructions (Table II, Group B). This group showed no correlation between the percentage of volatile bases, the duration of obstruction, or the condition of the experimental animal.

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toxicity occurring with a high pH was probably due to the liberation of ammonia, rather than to a direct action upon the intestine.

The results given in Table IV show quite conclusively that, when the distillate containing the volatile bases was removed from the intestinal fluid contents from the dogs dying with intestinal obstruction, the remaining portion did not elicit signs of toxicity when placed in intestinal loops of normal dogs. The pH of the residue was raised to a pH of 9 previous to injection in both experiments. When autopsied twenty-six and forty-eight hours later, the pH had dropped to 8.4 and 7.8 respectively.

The results obtained with the volatile basic distillate (Table V) were quite different. They showed that when the pH was set at a fixed level, the injected distillate caused early death in all animals.

TABLE V  
GROUP E.—TOXICITY OF DISTILLATE CONTAINING VOLATILE BASES

ANIMAL NO.	WEIGHT POUNDS	DISTILLATE INJECTED INTO CLOSED LOOP			LENGTH OF LOOP	DURATION AT DEATH HOURS	DEATH pH
		AMOUNT C.C.	pH	VOLATILE BASE PER CENT			
113	20	450	9+	0.485	Duodenum to lower ileum	5	-
114	45	400	9+	0.48	Duodenum to lower ileum	9	-
117	42	400	9+	0.37	Duodenum to lower ileum	4.5	8.8
128a	24	800	8.2	0.43	Esophagus to lower ileum	8 to 14	-
127b	36	800	9.0	0.43	Esophagus to lower ileum	3	-
135	28	500	About 8.6	0.43	Esophagus to lower ileum	24	-
138	48	1000	8.4	0.43	Duodenum to lower ileum	16	-

\*Blood CO<sub>2</sub> was 58 three or four hours following injection.

†Hydrogen ion concentration of urine was 7.1 just before death.

‡1,000 c.c. of the distillate was continuously irrigated through small intestine, being injected into a duodenal tube and collected by an ileal tube.

It must be concluded, therefore, that if the volatile bases of the fluid intestinal contents in low ileal obstruction occur in a certain concentration, death will occur, providing the H-ion concentration is at a certain level. This does not signify, however, that they are the primary cause of death in clinical intestinal obstruction.

#### SUMMARY AND CONCLUSION

An experimental study of the volatile bases developing in the fluid contents of the intestine following low ileal mechanical obstruction has been made. They were found to occur in concentrations varying from 0.14 per cent to 1.60 per cent. There appeared to be no correlation between the concentration of volatile bases, the duration of obstruction, or the condition of the experimental animal.



probably, if these investigators had taken into consideration not only the pH of the contents, but also the resistance that a normal dog would present as compared to a dehydrated dog with a seven-day obstructed intestine. In fact, a normal dog possesses the ability to lower the pH of a foreign intestinal fluid rapidly. This is shown in the following series of experiments, in which the toxicity of the intestinal contents obtained from dogs dying from intestinal obstruction was tested after the pH had been raised to an antemortem level. The length of life following injection in Dogs 50 and 130 was six and ten hours respectively. In Dog 50 the pH had dropped to 7.1 at death. In Dog 120, 300 c.c. of contents with pH raised to 7.8 was injected into a closed loop. For nine hours following the anesthesia, the dog was unable to stand and twitching of his tongue and neck was noticed. At twenty-four hours he would walk with a staggering gait and was extremely weak. From this time on he became worse, probably the result of the high obstruction. He was sacrificed at 50 hours and the pH of the intestinal fluid contents was 7.6.

#### TOXICITY OF $\text{NH}_3$ AND VOLATILE BASIC GROUP

In order to test the toxicity of the volatile bases a synthetic solution was used for injection into normal dogs. Since ammonia constituted about 50 per cent of the volatile basic group, it was prepared in a 1.75 per cent solution [ $\text{NH}_4\text{H CO}_3$  and  $(\text{NH}_4)_2\text{S}$ ] with a pH of 8.2 and injected into closed loops of otherwise normal dogs. After injection, the animals died in a very short time. A synthetic ammonia solution with a pH of less than 7 had no apparent untoward effect upon the experimental animals. In two experiments distilled water with the pH raised to 8.4 and to 9, with NaOH, then saturated with hydrogen sulphide and injected as before showed no ill-effects twenty and twenty-four hours later, respectively. By employing a solution containing the primary and tertiary amines in addition to ammonia, similar results would be expected since their toxicity increases in proportion to their complexity.

These results would suggest that the end-products of protein putrefaction were toxic only if the pH increased to a certain level. Since the pH influences the dissociation and solubility of ammonia salts, the

TABLE IV  
GROUP D.—TOXICITY OF VOLATILE BASE FREE RESIDUE

ANIMAL NO.	WEIGHT POUNDS	RESIDUE INJECTED INTO CLOSED LOOP			LENGTH OF LOOP	DURATION OF EXPERIMENT HOURS	pH AT DEATH
		AMOUNT C.C.	pH	VOLATILE BASE PER CENT			
134	30	500	9.0	0.038	Duodenum to Lower Ileum	26*	8.4
136	34	600	9.0	0.038	Esophagus to Lower Ileum	48*	7.8

\*Living and well when sacrificed.

toxicity occurring with a high pH was probably due to the liberation of ammonia, rather than to a direct action upon the intestine.

The results given in Table IV show quite conclusively that, when the distillate containing the volatile bases was removed from the intestinal fluid contents from the dogs dying with intestinal obstruction, the remaining portion did not elicit signs of toxicity when placed in intestinal loops of normal dogs. The pH of the residue was raised to a pH of 9 previous to injection in both experiments. When autopsied twenty-six and forty-eight hours later, the pH had dropped to 8.4 and 7.8 respectively.

The results obtained with the volatile basic distillate (Table V) were quite different. They showed that when the pH was set at a fixed level, the injected distillate caused early death in all animals.

TABLE V  
GROUP E.—TOXICITY OF DISTILLATE CONTAINING VOLATILE BASES

ANIMAL NO.	WEIGHT POUNDS	DISTILLATE INJECTED INTO CLOSED LOOP			LENGTH OF LOOP	DURATION AT DEATH HOURS	DEATH pH
		AMOUNT C.C.	pH	VOLATILE BASE PER CENT			
113	20	450	9+	0.485	Duodenum to lower ileum	5	-
114	45	400	9+	0.48	Duodenum to lower ileum	9	-
117	42	400	9+	0.37	Duodenum to lower ileum	4.5	8.8
128a <sup>*</sup>	24	800	8.2	0.43	Esophagus to lower ileum	8 to 14	-
127f	36	800	9.0	0.43	Esophagus to lower ileum	3	-
135	28	500	About 8.6	0.43	Esophagus to lower ileum	24	-
138f	48	1000	8.4	0.43	Duodenum to lower ileum	16	-

\*Blood CO<sub>2</sub> was 58 three or four hours following injection.

fHydrogen ion concentration of urine was 7.1 just before death.

11,000 c.c. of the distillate was continuously irrigated through small intestine, being injected into a duodenal tube and collected by an ileal tube.

It must be concluded, therefore, that if the volatile bases of the fluid intestinal contents in low ileal obstruction occur in a certain concentration, death will occur, providing the H-ion concentration is at a certain level. This does not signify, however, that they are the primary cause of death in clinical intestinal obstruction.

#### SUMMARY AND CONCLUSION

An experimental study of the volatile bases developing in the fluid contents of the intestine following low ileal mechanical obstruction has been made. They were found to occur in concentrations varying from 0.14 per cent to 1.60 per cent. There appeared to be no correlation between the concentration of volatile bases, the duration of obstruction, or the condition of the experimental animal.

The volatile bases were further analyzed for ammonia, primary, secondary, and tertiary amines. Ammonia consistently amounted to about 50 per cent of the group. The remaining half gave positive qualitative tests for primary and tertiary but negative reactions for secondary amines.

Although the volatile bases are products of protein putrefaction, a pure meat diet only slightly increased their concentration in the fluid contents of the obstructed intestine. The length of life in dogs obstructed at the ileocecal junction was greatly shortened when they were fed a pure meat diet in contrast to an ordinary or a meat-free diet.

When the pH of the intestinal contents obtained from dogs dying from intestinal obstruction was raised to an antemortem level and placed into bowel loops of normal animals, toxic symptoms appeared soon, followed by death of the experimental animals. Likewise, the distillate containing the volatile bases was found to possess the same characteristics.

In contradistinction to the toxic effects of the distillate, it has been shown that the action of the volatile base-free residue is entirely innocuous.

This does not necessarily signify that the volatile bases are the primary causes of death in intestinal obstruction, but it does mean that if they are present in a high enough concentration at an optimum pH and if they are absorbed, severe toxic symptoms will occur followed by a fatal outcome.

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## ACUTE INTESTINAL OBSTRUCTION

### I. THE RÔLE OF BACTERIA IN CLOSED JEJUNAL LOOPS

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OF THE various theories proposed to explain the cause of death in intestinal obstruction, two have received the most attention, viz.: (1) the loss of large amounts of fluids from the upper part of the gastrointestinal tract by vomiting; and (2) the absorption of some toxic substance formed in the obstructed bowel.

The serious consequences resulting from the loss of a large amount of fluid from the upper intestinal tract by vomiting have been repeatedly observed in both the experimental laboratory and in patients with acute bowel obstruction. In the experimental animal symptoms can be greatly altered and the length of life following acute obstruction definitely prolonged by the parenteral administration of adequate amounts of isotonic salt solution. Death, however, although delayed, is never prevented, and many workers feel that it is the absorption of some toxic material from the obstructed bowel which finally proves fatal.

Murphy and Brooks<sup>1</sup> and Dragstedt<sup>2</sup> found that closed intestinal loops were compatible with life if the bacteria in the loops were eliminated by adequate drainage before closure. If bacteria and tissue necrosis were present in the bowel segments, the animals died.

Williams,<sup>3</sup> in 1926, advanced the hypothesis that the Welch bacillus was the organism primarily responsible for the toxemia in intestinal obstruction. This conclusion was based on animal experiments carried out by methods which seem to us to be unsatisfactory and will be discussed later. Later workers have not been in agreement on this point.

Melver and others,<sup>4</sup> Oughterson and Powers,<sup>5</sup> and Thurston<sup>6</sup> were unable to find sufficient evidence that *Cl. welchii* was the important factor in acute intestinal obstruction, while the observations of Bower and Clark<sup>7</sup> as well as experiments by Morton and Stabins<sup>8</sup> seemed to show that *Cl. welchii* toxin played some part in the symptoms.

In the present experiments a study was made of the bacteriology and toxicity of the contents of obstructed bowel segments.

#### METHODS

Closed loops of upper jejunum were made in dogs under ether anesthesia. A portion of jejunum, varying from 15 to 30 cm. in length,

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The volatile bases were further analyzed for ammonia, primary, secondary, and tertiary amines. Ammonia consistently amounted to about 50 per cent of the group. The remaining half gave positive qualitative tests for primary and tertiary but negative reactions for secondary amines.

Although the volatile bases are products of protein putrefaction, a pure meat diet only slightly increased their concentration in the fluid contents of the obstructed intestine. The length of life in dogs obstructed at the ileocecal junction was greatly shortened when they were fed a pure meat diet in contrast to an ordinary or a meat-free diet.

When the pH of the intestinal contents obtained from dogs dying from intestinal obstruction was raised to an antemortem level and placed into bowel loops of normal animals, toxic symptoms appeared soon, followed by death of the experimental animals. Likewise, the distillate containing the volatile bases was found to possess the same characteristics.

In contradistinction to the toxic effects of the distillate, it has been shown that the action of the volatile base-free residue is entirely innocuous.

This does not necessarily signify that the volatile bases are the primary causes of death in intestinal obstruction, but it does mean that if they are present in a high enough concentration at an optimum pH and if they are absorbed, severe toxic symptoms will occur followed by a fatal outcome.

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A strain of *Cl welchii* was isolated from each animal. Identification of the organism was established by the characteristic stormy fermentation of milk, typical colonies on blood agar, and specific toxin production. The strains isolated were grown on chopped veal-beef infusion medium for toxin production in accordance with the procedure used by Bengston<sup>9</sup> at the National Institute of Health at Washington, D. C. It was necessary to transplant from a very young beef heart culture and incubate the culture for not longer than from sixteen to twenty-two hours to produce a potent toxin. The toxin was centrifugalized and filtered through a Berkefeld "N" candle before being used for injection. In each case the filtrate was cultured and found to be sterile. One group of mice was injected intravenously with 0.5 c.c. of this filtrate, and another group of animals was given 0.05 c.c. of *Cl. Welchii* antitoxin, previously mixed with the supernatant fluid and allowed to stand at room temperature for forty-five minutes.

## RESULTS

The results of the bacteriologic studies are presented in Table I. *Cl. welchii*, with one exception, was present in large numbers. The actual number of vegetative forms was probably much greater than

TABLE I  
PREDOMINATING ORGANISMS IN OBSTRUCTED LOOP FLUID\*

DOG	AEROBES	ANAEROBES
177	<i>B. aerogenes</i> 10 <sup>-9</sup> <i>B. coli</i> 10 <sup>-9</sup>	<i>Cl. welchii</i> 10 <sup>-4</sup>
181	<i>B. coli</i> 10 <sup>-11</sup> Fluid aspirated after 23 hours	<i>Cl. welchii</i> 10 <sup>-4</sup>
489	None Fluid aspirated after 97 hours None	<i>Cl. welchii</i> 10 <sup>-7</sup> <i>Cl. welchii</i> 10 <sup>-6</sup> Nonhem. gram + rods 10 <sup>-8</sup>
512	<i>B. coli</i> 10 <sup>-8</sup>	<i>Cl. welchii</i> 10 <sup>-6</sup>
261	<i>B. coli</i> 10 <sup>-11</sup>	<i>Cl. welchii</i> 10 <sup>-7</sup>
390	<i>B. coli</i> 10 <sup>-11</sup> <i>B. proteus</i>	<i>Cl. welchii</i> 10 <sup>-7</sup> Nonsporulating gram-rods
493	<i>B. coli</i> 10 <sup>-12</sup>	<i>Cl. welchii</i> 10 <sup>-6</sup>
526	<i>B. coli</i> 10 <sup>-10</sup>	Gram + bacilli (not <i>welchii</i> )
422	<i>B. coli</i> 10 <sup>-11</sup>	<i>Cl. welchii</i> 10 <sup>-2</sup>

\*Decimal dilutions expressed as exponents.

those recorded, since the method used detected only the number of spores. *B. coli* was usually present in large numbers also. Occasionally *B. aerogenes* and *B. proteus* were found, but in the majority of cases, *Cl. welchii* and *B. coli* completely predominated the flora. In one case, the Welch bacillus was the only organism isolated. Few anaerobic organisms other than *Cl. welchii* were ever encountered, although a search was made for these. The cocci were also conspicuously absent.

was sectioned at either end and the ends closed by purse-string sutures. The continuity of the bowel was reestablished by either a side-to-side or an end-to-end anastomosis. Following operation, the animals were placed in cages and given only water by mouth. When the animals appeared to be critically ill, usually thirty-six to seventy-two hours after operation, a second laparotomy was done and the obstructed loop removed. The fluid from this excised loop was immediately placed in sterile containers and used for bacteriologic examination and toxicity studies.

The loop contents were centrifugalized at high speed for forty-five minutes and the supernatant fluid carefully removed and used for mouse inoculations. Mice weighing from 17 to 20 gm. were given from 0.2 c.c. to 0.5 c.c. of fluid intravenously, control animals being given the same quantity together with 0.05 *Cl. welchii* antitoxin. Deaths of mice occurring within forty-eight hours only were recorded.

The following technique for culturing the loop fluid was selected because it seemed the best procedure for isolating as many types of bacteria as possible and for simultaneously determining quantitative relationships. Decimal dilutions of the loop fluid were made in tubes of sterile saline, from which lactose broth, Robertson's beef heart medium, and freshly boiled milk were inoculated.

Lactose broth was used to detect the presence of the coli-aerogenes group of bacteria. All lactose broth cultures giving the reaction of *B. coli* were streaked out on eosin-methylene blue agar plates for final identification. Beef heart medium was used because it satisfied the growth requirements of the gram-negative intestinal bacteria, the cocci, and many of the sporulating and nonsporulating anaerobes. The cultures were incubated one week. The highest dilutions showing growth in beef heart medium were used for inoculating aerobic and anaerobic blood agar plates. Identification of the predominating types of bacteria was made from these.

Milk was used for the estimation of the numbers of *Cl. welchii*. The inoculum was heated at 80° C. for ten minutes. The cultures were incubated in an anaerobic jar, and when typical stormy fermentation occurred, they were removed from the jar and blood agar plates were streaked for the isolation of *Cl. welchii*. This method gives only an estimate of the number of spores present; the number of vegetative forms, perhaps, is much greater.

The 1:10 dilution of loop fluid was used for direct inoculation of blood agar and eosin-methylene blue agar plates. Blood agar plates were incubated anaerobically at a temperature of 37° C. for four days. Aerobic blood agar and eosin-methylene blue plates were incubated for twenty-four hours. Identification of the predominating organisms on these plates was then made.

## DISCUSSION

Williams mixed the contents of the small intestine with an equal amount of ice cold saline solution and passed this through a Berkefeld candle in an atmosphere of hydrogen in the ice chest. The filtration always took from eighteen to twenty-four hours. Mice were injected intramuscularly, using 0.75 c.c. of filtrate plus 0.25 c.c. of normal horse serum in one series, and 0.75 c.c. of filtrate together with 0.25 c.c. of *Cl. welchii* antitoxin in another series. Striking results were tabulated, showing large numbers of deaths in the first group and no fatalities in the protected group. The mice were kept under observation for six days. All the mice which died were examined for the possibility of infection with *Cl. welchii*, as opposed to toxemia, by heart blood cultures taken as soon after death as possible. He states that all these cultures were negative as regards *Cl. welchii*, although occasionally streptococci and coliforms were found. Assuming that examination was made soon enough after death to prevent the possibility of postmortem invasion of organisms, his results indicate that the filtrates were not sterile.

It seems logical that the intramuscular injection of quantities as large as 1 c.c. into a mouse could produce enough tissue injury to afford conditions suitable for the elaboration of a toxin by the Welch bacillus, if that organism were contained in the fluid injected. The fact that the filtrates Williams used were not sterile seems to indicate that *Cl. welchii* may have been present in the filtrates. Despite his failure to demonstrate *Cl. welchii* in the heart blood, the organisms would, more likely, have localized at the site of injection. It is possible that the mice died from a toxin elaborated by *Cl. welchii* in the tissues rather than from any toxin contained in the loop fluid. Williams kept the mice under observation for six days. Our experience, and that of others<sup>9, 10</sup> has been that intravenous injection of a potent toxin of *Cl. welchii* in quantities much less than 1 c.c. will kill a mouse in from two to forty-eight hours. Death of mice after forty-eight hours may be attributed to other causes.

McIver and others are of the opinion that the strains of *Cl. welchii* found in the intestinal tract are of a low degree of virulence and are not good toxin producers. The strains studied here, with two exceptions (Dogs 390 and 493), all produced toxin when grown in a suitable medium for from sixteen to twenty-four hours. It was found that the use of old cultures for inoculation of the chopped veal medium gave poor results, and that the time of incubation of cultures for the production of toxin was important and varied considerably.

Wilsdon<sup>11</sup> has recently divided the *Cl. welchii* group into four types, each differing in the antigenic structure of the toxin produced. Types A, B, and C produced the maximum of toxin within twenty-four hours. However, Type D, consisting of a series of strains of animal origin, pro-



TABLE II

EVIDENCE FOR THE PRESENCE OF *Cl. welchii* TOXIN IN THE OBSTRUCTED LOOP FLUID.  
TOXIN PRODUCING CAPACITY IN VITRO OF *Cl. welchii* ORGANISMS ISOLATED  
FROM THE OBSTRUCTED LOOP CONTENT

DOG	RESULTS OF INOCULATION WITH LOOP FLUID				IN VITRO PRODUCTION OF TOXIN BY HOMOLOGOUS STAINS	
	TEST MICE		ANTITOXIN CONTROLS		TEST MICE*	
	NO. OF DEATHS	NO. OF SURVIVALS	NO. OF DEATHS	NO. OF SURVIVALS	NO. OF DEATHS	NO. OF SURVIVALS
177	0	5	1	4	2	1
181	4	1	1	4	3	0
Fluid aspirated after 23 hours						
489	0	5	0	4	3	0
Fluid aspirated after 97 hours (end of experiment)						
	0	4	0	5		
512	1	1	1	0	2	0
261	1	1	2	0	3	0
390	4	0	2	3	No toxin demonstrated	
493	3	1	3	0		
526	3	1	2	1		

\*Antitoxin controls all survived.

The results of the toxicity studies are presented in Table II. No conclusive evidence of the presence of *Cl. welchii* toxin in the loop fluid was found. The method for preparing the fluid for mouse injection is open to criticism in that the fluid was not sterile. Prolonged filtration, which is necessary with this type of material, and heating may be destructive to *Cl. welchii* toxin, and for that reason were avoided. However, the survival of the mice in some of these experiments is evidence against the presence of welchii toxin. If the fluid contained a toxic entity, such as *C. welchii* toxin, one would expect uniform deaths among the animals injected in a short period of time. This was not the case in these experiments.

The strains of the Welch bacillus isolated from each loop, with two exceptions, were good toxin producers when grown in suitable medium. In one experiment none of the mice receiving loop fluid died. This fluid, however, contained one of the best toxin-producing strains which was encountered.

In two instances (Dogs 181 and 489) blood was drawn three weeks after obstruction to test for the presence of *Cl. welchii* antitoxin. Mice injected with 0.5 c.c. of filtrate (prepared with homologous strains) mixed with 0.1 c.c. of the blood serum of the dog and allowed to stand at room temperature for forty-five minutes before injection, all died.

Bull and Pritchett<sup>10</sup> have shown that young cultures of *Cl. welchii* contain the maximum of toxin, and that with prolonged incubation, the toxicity decreases. With this idea in mind, fluid was aspirated from an intestinal loop (Dog 489) twenty-three hours after obstruction and tested for toxin. None of the mice receiving the fluid died.

## ACUTE INTESTINAL OBSTRUCTION

### II. THE PERMEABILITY OF OBSTRUCTED BOWEL SEGMENTS OF DOGS TO *Clostridium botulinum* TOXIN

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THE rôle played by bacteria and their products in intestinal obstruction is an unsettled problem. This subject has been discussed in a previous report. The permeability of the obstructed bowel has been studied by other workers with regard to some of the chemical poisons, but no satisfactory method has been devised to study the permeability to bacterial products. Since the dog was known to be quite resistant to oral administration of botulinum toxin and since this toxin is of bacterial origin, it was thought that this substance might better meet the conditions found in intestinal obstruction. Furthermore, this is one of the most potent bacterial toxins and can be detected in very small quantities.

Cultures of *Cl. botulinum* Type A were grown in Kjeldahl flasks containing Robertson's beef heart medium under a vaseline-paraffin seal. These were incubated at 37° C. for from four to fourteen days, at the end of which time the supernatant fluid was centrifugalized at high speed for one-half hour. The resulting supernatant fluid was pipetted off carefully and constituted the toxin used in these experiments. The potency of the toxin was determined by intraperitoneal injections of 1 c.c. of decimal dilutions into each of two mice, weighing from 17 to 20 grams each. The mice were kept on test for forty-eight hours. The same procedure was used for detection of toxin in the blood serum of dogs. Control mice were inoculated with 0.25 c.c. of *Cl. botulinum* antitoxin.

#### I. PERMEABILITY OF NORMAL BOWEL SEGMENTS

To determine whether the normal dog intestine was permeable to *Cl. botulinum* toxin, 20 dogs were fed varying quantities of highly potent botulinum toxin\* with a stomach tube. Four dogs fed 25 c.c. and 4 dogs fed 50 c.c. gave no evidence that absorption was obtained. A variation in results occurred when 100 c.c. quantities were fed. In 2 out of 12 dogs fed from 85 to 100 c.c., there was no absorption of toxin.

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\*Titrations of toxin used in feeding experiments were comparable with those used in later obstruction experiments.

duced a toxin which did not reach its maximum for three to five days. This may explain our failure to obtain toxins with strains isolated from Dogs 390 and 493.

#### SUMMARY AND CONCLUSIONS

Bacteriologic studies were made on the fluid obtained from closed intestinal loops in eight dogs.

*Cl. welchii* and *B. coli* were found to be the predominating organisms. In most instances the Welch organisms were shown to be capable of producing a potent toxin in vitro. No definite evidence of *Cl. welchii* toxin in the loop fluid was demonstrated.

The present study does not substantiate the view that the toxemia of acute intestinal obstruction is due to the specific toxin of the Welch bacillus.

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## ACUTE INTESTINAL OBSTRUCTION

### II. THE PERMEABILITY OF OBSTRUCTED BOWEL SEGMENTS OF DOGS TO *Clostridium botulinum* TOXIN

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THE rôle played by bacteria and their products in intestinal obstruction is an unsettled problem. This subject has been discussed in a previous report. The permeability of the obstructed bowel has been studied by other workers with regard to some of the chemical poisons, but no satisfactory method has been devised to study the permeability to bacterial products. Since the dog was known to be quite resistant to oral administration of botulinum toxin and since this toxin is of bacterial origin, it was thought that this substance might better meet the conditions found in intestinal obstruction. Furthermore, this is one of the most potent bacterial toxins and can be detected in very small quantities.

Cultures of *Cl. botulinum* Type A were grown in Kjeldahl flasks containing Robertson's beef heart medium under a vaseline-paraffin seal. These were incubated at 37° C. for from four to fourteen days, at the end of which time the supernatant fluid was centrifugalized at high speed for one-half hour. The resulting supernatant fluid was pipetted off carefully and constituted the toxin used in these experiments. The potency of the toxin was determined by intraperitoneal injections of 1 c.c. of decimal dilutions into each of two mice, weighing from 17 to 20 grams each. The mice were kept on test for forty-eight hours. The same procedure was used for detection of toxin in the blood serum of dogs. Control mice were inoculated with 0.25 c.c. of *Cl. botulinum* antitoxin.

#### I. PERMEABILITY OF NORMAL BOWEL SEGMENTS

To determine whether the normal dog intestine was permeable to *Cl. botulinum* toxin, 20 dogs were fed varying quantities of highly potent botulinum toxin\* with a stomach tube. Four dogs fed 25 c.c. and 4 dogs fed 50 c.c. gave no evidence that absorption was obtained. A variation in results occurred when 100 c.c. quantities were fed. In 2 out of 12 dogs fed from 85 to 100 c.c., there was no absorption of toxin.

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\*Titrations of toxin used in feeding experiments were comparable with those used in later obstruction experiments.

duced a toxin which did not reach its maximum for three to five days. This may explain our failure to obtain toxins with strains isolated from Dogs 390 and 493.

#### SUMMARY AND CONCLUSIONS

Bacteriologic studies were made on the fluid obtained from closed intestinal loops in eight dogs.

*Cl. welchii* and *B. coli* were found to be the predominating organisms. In most instances the Welch organisms were shown to be capable of producing a potent toxin in vitro. No definite evidence of *Cl. welchii* toxin in the loop fluid was demonstrated.

The present study does not substantiate the view that the toxemia of acute intestinal obstruction is due to the specific toxin of the Welch bacillus.

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with an M.L.D. of at least  $10^{-4}$  was used, the dog died and toxin was demonstrated in the blood serum in six hours (no titrations were made earlier). Further experiments demonstrated that when 3 c.c. of potent toxin is administered intraperitoneally, the toxin enters the blood within two hours, increases in amount with time, and is fatal to the dog. The negative results obtained in Case 4 may possibly be explained by the toxin entering a viscus instead of the peritoneum. The same toxin was used in Case 5 with fatal results.

### III. ACUTE INTESTINAL OBSTRUCTION EXPERIMENTS

Dogs were prepared with isolated loops of small intestine, the ends carefully infolded by means of purse-string sutures, and the continuity of the intestinal tract reestablished by means of end-to-end anastomoses. *Cl. botulinum* toxin was inoculated into the loop with a fine needle, care being taken to prevent any toxin from entering the peritoneal cavity. The loop was put back into the peritoneum and the incision closed. Blood was drawn at intervals and the serum inoculated into white mice to test for the presence of *Cl. botulinum* toxin. The results are presented in Table II.

TABLE II

BOTULINUM TOXIN IN BLOOD SERUM OF DOGS RECEIVING 10 C.C. OF TOXIN INTO OBSTRUCTED LOOPS OF SMALL INTESTINE

DOG	M.L.D. OF TOXIN	DILU- TION OF SERUM	TOXIN IN BLOOD SERUM					HEART BLOOD AT DEATH
			3-6 HR.	16-18 HR.	20-24 HR.	30 HR.		
<i>Acute Obstruction Experiments</i>								
8	10-4+	0		--				++
	10-5-	1:10		--				-- (36 hr.)
9	10-3+	0	--	--		--	Experiment Discontinued	
	10-4-	1:10	--	--		--		
10	2 x 10-4+	0	--	--	+			++
	10-4-	1:10	--	--				++ (60 hr.)
<i>Obstructed Loops Previously Drained</i>								
11	10-3+	0	--		--	--	++	++
	10-4-	1:10	--		--	--	++	++
12	10-3+	0	--		--	--	(40 hr.)	(64½ hr.)
	10-4-	1:10	--		--	--	--	(69½ hr.)
		1:50				--	--	++
						(40 hr.)	(63¾ hr.)	++
<i>Obstructed Loop Previously Washed with Tannic Acid Toxin Inoculated After Obstruction Began</i>								
13	10-4+	0	++	++	++			
	10-5-	1:10	--	+-	++			
		1:100	--	--	++			

+ denotes death of 1 mouse; - denotes survival of 1 mouse; blank space, test not made.

Absorption was questionable in 4 other animals fed 100 c.c. (antitoxin controls died in 2 of these). When 2 other animals were fed, considerable bleeding about the mouth occurred, and this is thought to have been responsible for the early death of the dog and ready absorption of toxin. In subsequent feedings, the dogs were put under light ether anesthesia. This eliminated struggling and avoided abrasions in the oral mucosa.

In 4 other dogs fed 100 c.c. of potent toxin, absorption was demonstrated, but in only 1 of these was it sufficient to cause the death of the animal (died nine days after feeding). Furthermore, the toxin in these 4 animals was never absorbed in quantities sufficient to be detected by mouse injection in a 1:10 dilution of the serum. However, toxin was sometimes demonstrated in this dilution in the experiments with acute obstruction of loops of the small intestine.

## II. ABSORPTION OF *Cl. Botulinum* TOXIN FROM THE PERITONEAL CAVITY OF DOGS

Dogs were given intraperitoneal inoculations of toxin to determine the time of appearance in the blood and to gain some quantitative relationship between potency of toxin and amount absorbed. Results are recorded in Table I. Two dogs, Cases 2 and 3, were inoculated with 3 c.c.

TABLE I

BOTULINUM TOXIN IN BLOOD SERUM OF DOGS INJECTED INTRAPERITONEALLY WITH 3 C.C. OF TOXIN

DOG	M.L.D. OF TOXIN	DILUTION OF SERUM	TOXIN IN BLOOD SERUM					RESULTS OUTCOME FOR DOG
			2 HR.	4-4½ HR.	6-6½ HR.	12 HR.	24 HR.	
1	10 <sup>-4</sup> +	0			++	++	++	Fatal
	*	1:10			++	++	++	
2	10 <sup>-3</sup> +	0	--	--	--			Survived
	10 <sup>-4</sup> -	1:10	--	--	--			
3	10 <sup>-3</sup> +	0	--	--	--			Survived
	10 <sup>-4</sup> -	1:10	--	--	--			
4	2 × 10 <sup>-4</sup> +	0	--	--	--			Survived
	10 <sup>-4</sup> -	1:10	--	--	--			
5	2 × 10 <sup>-4</sup> +	0	++	++	++			Fatal
	10 <sup>-4</sup> -	1:10	--	+-	++			
6	10 <sup>-4</sup> +	0	++	++	++			Fatal
	*	1:10	++	++	++			
7		1:100		+-	+-			Fatal
	10 <sup>-4</sup>	0	++	++	++			
	*	1:10	++	++	++			
		1:100		--	+-			

+ denotes death of 1 mouse; - denotes survival of 1 mouse; \*, not tested in a dilution greater than 10<sup>-4</sup>; blank space, no test made.

of filtered toxin with the M. L. D.\* varying between 10<sup>-3</sup> to 10<sup>-4</sup>. No toxin was demonstrated in the blood serum of these two animals, and they survived with no ill effects. In Case 1 where a nonfiltered toxin

\*M. L. D. determined roughly by decimal dilutions of toxin injected intraperitoneally into white mice.

with an M.L.D. of at least  $10^{-4}$  was used, the dog died and toxin was demonstrated in the blood serum in six hours (no titrations were made earlier). Further experiments demonstrated that when 3 c.c. of potent toxin is administered intraperitoneally, the toxin enters the blood within two hours, increases in amount with time, and is fatal to the dog. The negative results obtained in Case 4 may possibly be explained by the toxin entering a viscus instead of the peritoneum. The same toxin was used in Case 5 with fatal results.

### III. ACUTE INTESTINAL OBSTRUCTION EXPERIMENTS

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TABLE II

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			3-6 HR.	16-18 HR.	20-24 HR.	30 HR.		
<i>Acute Obstruction Experiments</i>								
8	10 <sup>-4+</sup>	0		--				++
	10 <sup>-5-</sup>	1:10		--				--
9	10 <sup>-3+</sup>	0	--	--		--	Experiment Discontinued	(36 hr.)
	10 <sup>-4-</sup>	1:10	--	--		--		
10	2 × 10 <sup>-4+</sup>	0	--	--	+			++
	10 <sup>-4-</sup>	1:10	--	--				++ (60 hr.)
<i>Obstructed Loops Previously Drained</i>								
11	10 <sup>-3+</sup>	0	--		--	--	++	++
	10 <sup>-4-</sup>	1:10	--		--	--	++	++
12	10 <sup>-3+</sup>	0	--		--	--	(40 hr.)	(64½ hr.)
	10 <sup>-4-</sup>	1:10	--		--	--	--	++
		1:50				(40 hr.)	(63¾ hr.)	++
<i>Obstructed Loop Previously Washed with Tannic Acid Toxin Inoculated After Obstruction Began</i>								
13	10 <sup>-4+</sup>	0	++	++	++			
	10 <sup>-5-</sup>	1:10	--	+-	++			
		1:100	--	--	++			

+ denotes death of 1 mouse; - denotes survival of 1 mouse; blank space, test not made.



In Case 8 the dog died in thirty-six hours. Toxin was demonstrated in the heart blood serum and in the loop contents. The pathologic picture was not typical of acute obstruction, the loop contained no fluid (solid fecal material only) and was not noticeably distended. This suggests that the death may have been due to factors other than obstruction. The possibility suggests itself that some of the toxin may have leaked from the infolded ends of the loop. Were this the case, one would expect to find toxin in the blood serum at an early stage, if



Fig. 1.—Dog 271; photograph of x-ray taken three days after obstruction.

the results from the intraperitoneal inoculations are taken into consideration. No toxin was demonstrated in Case 8 before the death of the animal (thirty-six hours).

In Case 9 the toxin was discovered to be of low titer after the dog had been inoculated. No toxin was demonstrated in the blood serum within thirty hours, and, when the dog became ill, the loop was removed to save the animal. No further titrations were made on the blood serum, but toxin was found in a specimen from the isolated loop.

Dog 10 died in sixty hours. The loop had perforated. This perforation was apparently quite recent since there was still considerable fluid in the loop. Blood drawn twenty-four and a half hours after inoculation contained some toxin as did the heart blood in a 1:10 dilution.

#### IV. PERMEABILITY OF *Cl. Botulinum* TOXIN FROM ISOLATED LOOPS PREPARED FROM THIRY FISTULAS

Dogs were prepared with isolated loops of jejunum closed at one end, the other open end brought to the outside through a stab wound in the abdominal wall. The loops were permitted to drain for eight months



Fig. 2.—Dog 597; photograph of x-ray taken seven days after operation.

and then were carefully closed from within. At this time they appeared much atrophied. In Cases 11 and 12, 10 c.c. of botulinum toxin were injected into the loop after closure. The results are recorded in Table II.

As may be seen from the table, toxin was found in the dog blood in Case 11, a few hours before death. In Case 12 the toxin was found in the heart blood taken shortly after death, but none was found in the serum twenty-three hours before death. Blood cultures were made each time blood was drawn to check on the possibility of septicemia resulting from rupture of the loop. All cultures remained sterile with the exception of one made from blood taken very shortly after death of the animal.

A third dog received no botulinum toxin. Cultures of the loop made before closure showed no growth. The dog died in eight days. A pure culture of hemolytic streptococci was obtained from the loop fluid. This fluid was not toxic for mice.

#### V. EXPERIMENTS WITH ISOLATED LOOPS OF INTESTINE WASHED WITH TANNIC ACID BEFORE CLOSURE

Two dogs were prepared with isolated loops of jejunum, washed with a 6 per cent solution of tannic acid before closure, the purpose being to minimize secretion and distention before the infolded loops had healed. One dog died from peritonitis, and the second dog was allowed to go for three days, at which time a second laparotomy was performed. The loop was very distended and darkened in a few areas. Two hundred cubic centimeters of brownish fluid were aspirated, and hot packs were applied to the loop until peristalsis had returned and the circulation appeared good with the exception of a few areas opposite the mesenteric attachment. Ten cubic centimeters of botulinum toxin were injected into the loop. The results are tabulated in Table II.

From the one experiment which was carried to completion, it may be seen that the toxin readily passed through the damaged intestinal wall. There was some leakage from the syringe when the toxin was injected, but the amount was calculated as too small to be detected in the general circulation by mouse injection.

#### VI. RELATIONSHIP OF ABSORPTION OF TOXIN AND DISTENTION OF THE ISOLATED LOOPS OF BOWEL

To correlate the absorption of botulinum toxin with the degree of distention of the isolated intestinal segments, the following experiments were undertaken. Dogs were prepared with isolated loops of ileum into which 10 c.c. of *Cl. botulinum* toxin and 20 c.c. of barium sulfate solution were carefully injected before closure of the abdomen. The animals were x-rayed following the operation, and at the time a blood specimen was drawn for toxin titrations.

X-ray pictures were always made on the same scale and by this procedure, the size of the loop could be followed easily. Contraction due to peristaltic movements sometimes complicated the picture, but, in general, the increase or lack of increase in size could be readily determined. Photographs of two such x-rays are shown in Figs. 1 and 2. Tracings of the x-rays were made and are shown in Figs. 3 to 13. Results of the toxin assays are presented in Table III.

No toxin was demonstrated in the blood serum of 5 of the 11 dogs studied in this manner. The toxin used in one experiment (Dog 316) was found to be of a very low titer, and, although there was a gradual and marked distention of the isolated loop, no toxin could be detected

TABLE III  
BOTULINUM TOXIN IN BLOOD SERUM OF DOGS RECEIVING 10 C.C. OF BOTULINUM TOXIN AND 20 C.C. OF BARIUM SULFATE SOLUTION INTO OBSTRUCTED LOOPS OF ILEUM

DOG	M.L.D. OF TOXIN	DILUTION OF SERUM	TOXIN IN BLOOD SERUM AFTER								TOXIN IN LOOP AT DEATH OF DOG*
			1 DAY	2 DAYS	3 DAYS	4 DAYS	5 DAYS	6 DAYS	7 DAYS	8 DAYS (OR MORE)	
316	10-1 + 10-2 -	0 1:10	- - - -	- - - -	- - - -	- - - -	- - - -	- - - -	- - - -	- - 11 days ==	Not tested
338	10-4 + 10-5 -	0 1:10	- - - +	- - Death of dog	- - - -	- - - -	- - - -	- - - -	- - - -	- - - -	+
391	10-4 + 10-5 -	0 1:10	- - - -	- - Death of dog	- - - -	- - - -	- - - -	- - - -	- - - -	- - - -	Not tested
586	10-5 + 10-6 -	0 1:10	- - - -	- - Death of dog	- - - -	- - - -	- - - -	- - - -	- - - -	- - - -	Not tested
611	10-4 + 10-5 -	0 1:10	+ - - -	- - Dog died— distemper	- - - -	- - - -	- - - -	- - - -	- - - -	- - - -	+
319	10-5 + 10-6 -	0 1:10	- - - -	- - - -	- - - -	- - - -	- - - -	- - - -	- - - -	- - - -	Not tested
501	10-5 + 10-6 -	0 1:10	+ + - -	+ + - -	Death of dog + + +	- - - -	- - - -	- - - -	- - - -	- - - -	Not tested
388	10-4 + 10-5 -	0 1:10	+ - - -	- - - -	- - - -	+ + + +	+ + + +	+ + + +	+ + + +	+ + + +	+
271	10-5 + 10-6 -	0 1:10	- - - -	- - - -	- - - -	+ + + +	+ + + +	+ + + +	+ + + +	+ + + +	+
621	10-5 + 10-6 -	0 1:10	- - - -	+ + - -	+ - - -	+ - + +	+ + + +	+ + + +	+ + + +	Death of dog + - - - + + + + + + + +	-
597	10-5 + 10-6 -	0 1:10	- - - -	- - - -	- - - -	+ + + +	+ + + +	+ + + +	+ + + +	+ + + + Dog killed 12th day	+

\*Determined by guinea pig feeding experiments.

+ denotes death of 1 mouse; - denotes survival of 1 mouse; blank space, not tested.

A third dog received no botulinum toxin. Cultures of the loop made before closure showed no growth. The dog died in eight days. A pure culture of hemolytic streptococci was obtained from the loop fluid. This fluid was not toxic for mice.

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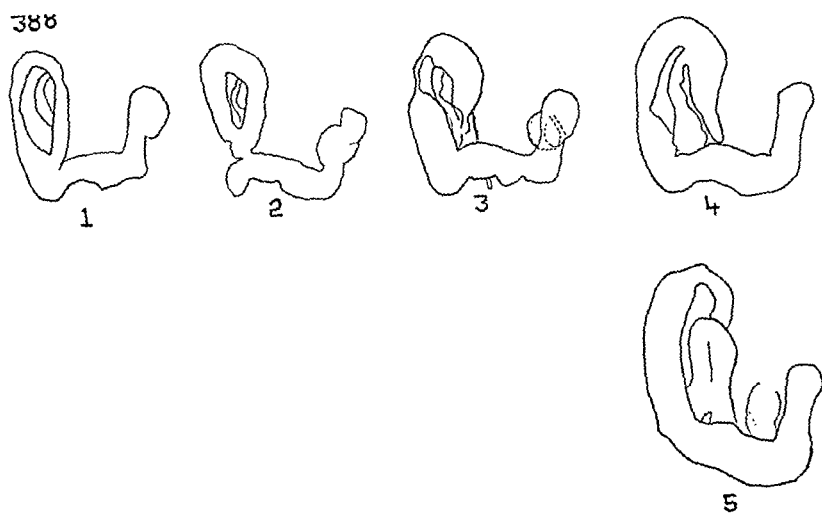
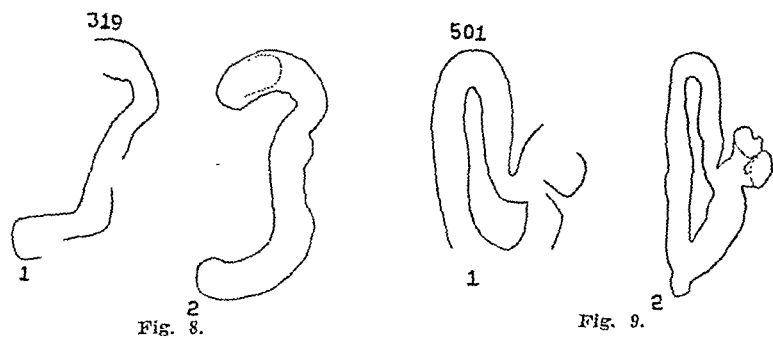


Fig. 10.

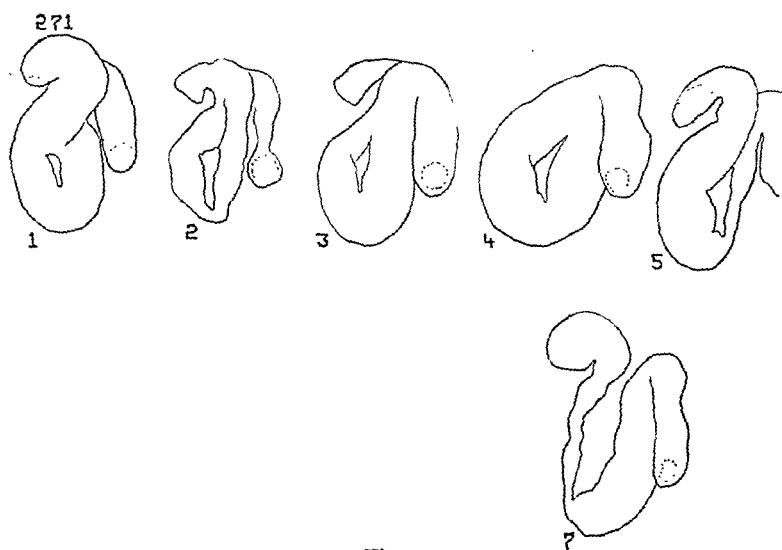


Fig. 11.

FIGS. 8-11 —See opposite page for legend.

in the blood stream. The remaining 4 animals died within forty-eight hours, and in only 1 was there any distention of the isolated loop.

Evidence of absorption was obtained in 6 of the 11 dogs, and this was usually concomitant with the distention of the isolated loops. In the case of Dog 319 no toxin was found in the blood until after the



Fig. 3.

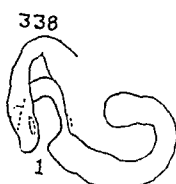


Fig. 4.

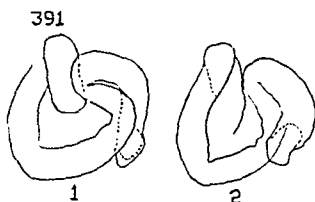


Fig. 5.

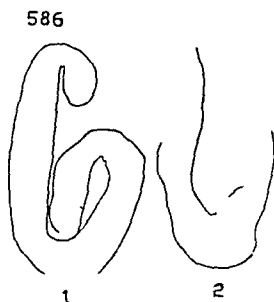


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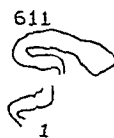


Fig. 7.

Figs. 3-13.—Tracings of x-rays. Numbers placed below each loop in Figs. 3 through 13 indicate the number of days after obstruction was produced.

death of the dog, although the loop was shown to have increased in size after forty-eight hours. At autopsy it was found that the loop had ruptured and the absorption of toxin noted at death was, in all probability, directly from the peritoneal cavity.

Dog 501 died in three days. Autopsy revealed a generalized peritonitis and a rupture (apparently quite recent) in the loop which cor-

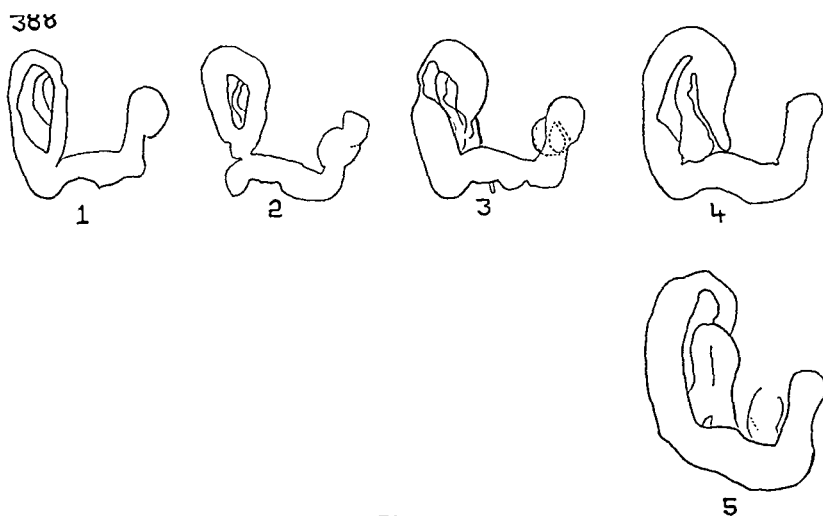
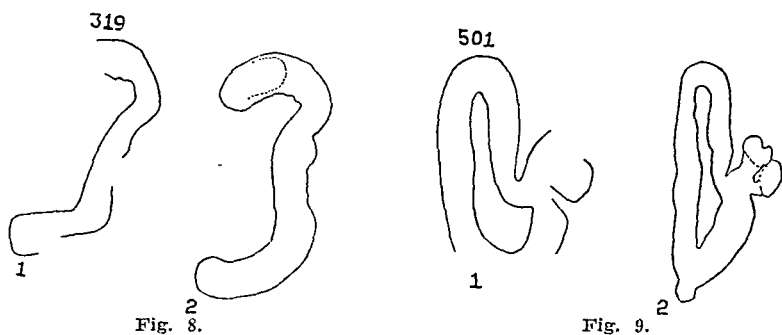


Fig. 10.

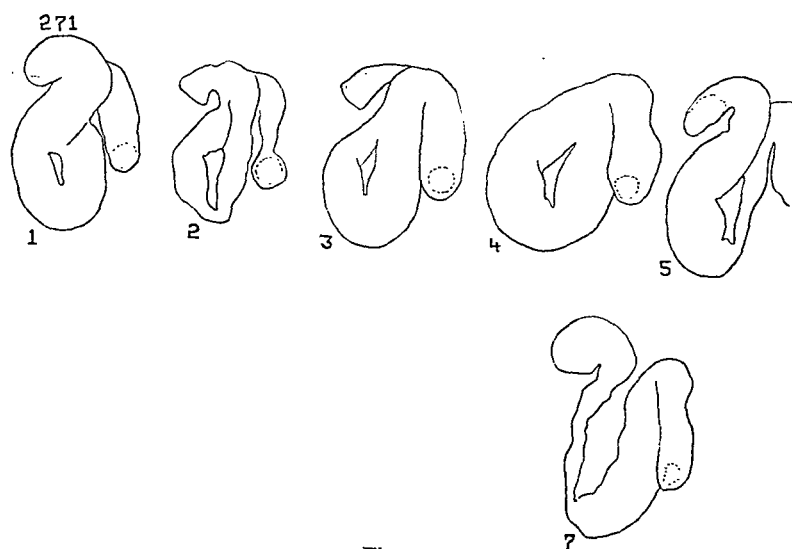


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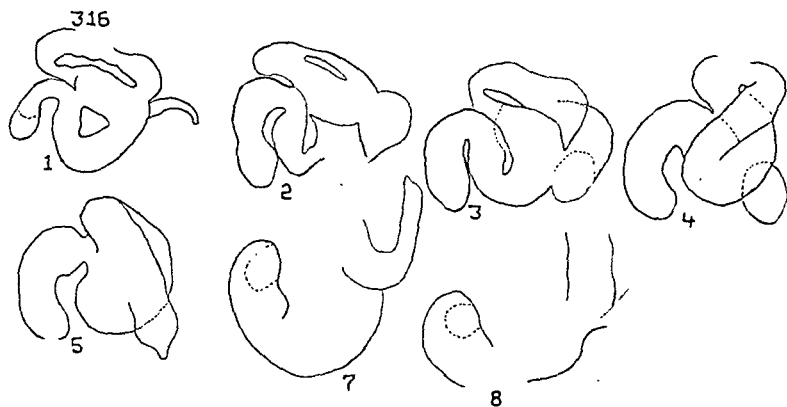


Fig. 3.

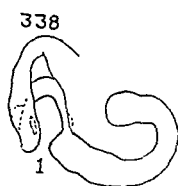


Fig. 4.

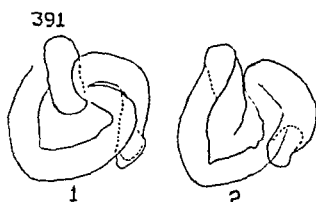


Fig. 5.

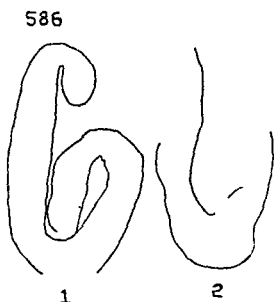


Fig. 6.

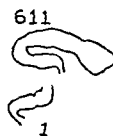


Fig. 7.

Figs. 3-13.—Tracings of x-rays. Numbers placed below each loop in Figs. 3 through 13 indicate the number of days after obstruction was produced.

death of the dog, although the loop was shown to have increased in size after forty-eight hours. At autopsy it was found that the loop had ruptured and the absorption of toxin noted at death was, in all probability, directly from the peritoneal cavity.

Dog 501 died in three days. Autopsy revealed a generalized peritonitis and a rupture (apparently quite recent) in the loop which cor-

Blood drawn from Dog 271 on the third, fourth, and fifth days after operation contained toxin. The serum was not toxic on the sixth day. Unfortunately no x-ray picture was obtained that day. On the seventh day presence of toxin was questionable, although the x-ray showed the loop to be enormously distended. The quantity of toxin in the serum of Dog 597 appeared to decrease after the seventh day. Pictures of the loop show that it decreased steadily in size after the tenth day.

#### DISCUSSION

Little is known about the absorption of toxin products from obstructed loops of the bowel. The reason for this lack of knowledge is due to the difficulties of assaying many of the toxic metabolic products formed by the enormous number of bacteria multiplying in the obstructed intestinal tract. The permeability to dyes and to chemical poisons does not offer a parallel situation to what naturally happens. It appeared to us that the toxin of *Cl. botulinum* was particularly well adapted to this type of experimentation, since it is a poison produced by bacteria; it is of sufficient potency so that very small amounts can be detected by the intraperitoneal injection of white mice, some of which have been protected with homologous antitoxin.

Fortunately the dog has considerable resistance to this toxin as evidenced by the fact that 100 c.c. of a potent toxin may be fed to dogs with impunity; whereas, a fraction of 1 c.c. is lethal for man, monkeys, and guinea pigs. This resistance enables the dogs to survive for a long time when a lethal dose of toxin for the white mouse (intraperitoneal route) is present in each cubic centimeter of dog's blood. Another advantage to the use of botulinum toxin was that the toxin is not readily destroyed in the contents of the isolated loop of bowel.

Our experiments indicate that the toxin of *Cl. botulinum*, which in moderate quantities is not absorbed from the normal intestinal tract of dogs, is readily absorbed from obstructed bowel segments. The results strongly indicate that when distention occurs, the toxin enters the blood stream. The possibility that the toxin may have leaked from the loops or may have been absorbed from the loop ends is precluded in view of the fact that it took a long time for it to be detected in the blood when introduced into isolated loops of bowel; whereas, toxin introduced intraperitoneally can be demonstrated in as short a period as two hours.

#### SUMMARY AND CONCLUSIONS

1. *Cl. botulinum* toxin has not been demonstrated to pass through the normal intestinal wall of dogs when fed in quantities of 50 c.c. or less. Feeding of larger quantities occasionally resulted in absorption, but never in large amounts.

responded to the outpouching evident in the x-ray taken on the second day after operation. Toxin was found to be present in the blood stream twenty-four and again forty-eight hours after operation.

In 4 of the animals rather clear cut evidence of absorption of toxin into the blood stream was obtained when distention of the loop occurred. In Dog 388 death occurred on the sixth day after operation. X-ray

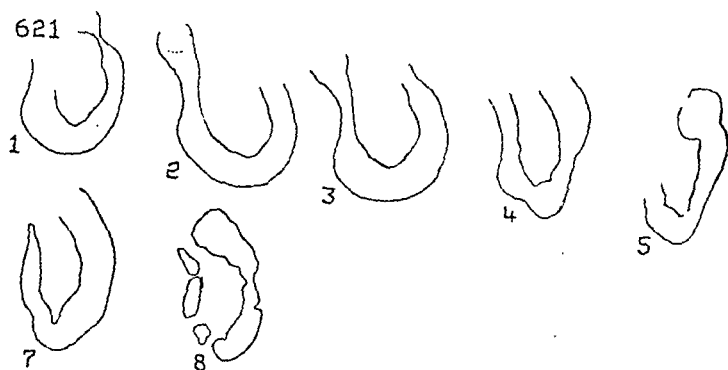


Fig. 12.

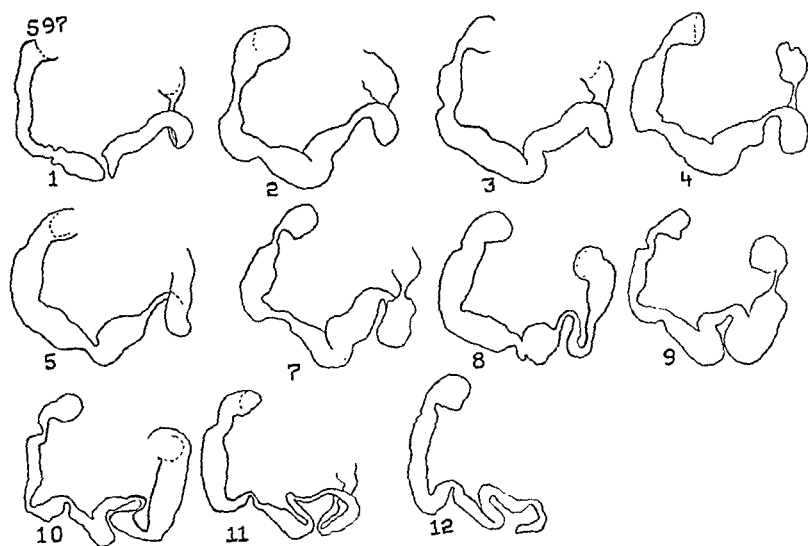


Fig. 13.

Figs. 12 and 13.—See page 346 for legend.

pictures revealed a steady increase in size of the loop each day, and a steady increase of botulinum toxin was found in the serum. It may be noted that in Dog 621, the greatest amount of toxin was found four days after obstruction, after which time it decreased steadily. From the x-ray pictures one may note that the distention was greater on the third day, after which it decreased until the eighth day.

Blood drawn from Dog 271 on the third, fourth, and fifth days after operation contained toxin. The serum was not toxic on the sixth day. Unfortunately no x-ray picture was obtained that day. On the seventh day presence of toxin was questionable, although the x-ray showed the loop to be enormously distended. The quantity of toxin in the serum of Dog 597 appeared to decrease after the seventh day. Pictures of the loop show that it decreased steadily in size after the tenth day.

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#### SUMMARY AND CONCLUSIONS

1. *Cl. botulinum* toxin has not been demonstrated to pass through the normal intestinal wall of dogs when fed in quantities of 50 c.c. or less. Feeding of larger quantities occasionally resulted in absorption, but never in large amounts.

2. This toxin injected intraperitoneally, in suitable doses, is readily absorbed into the blood stream. The toxin may be demonstrated in the blood within two hours; it increases in quantity with time, and is lethal to the dog.

3. Absorption of *Cl. botulinum* toxin placed in small quantities in obstructed segments of the small intestine of dogs has been demonstrated. The distention of the isolated loops was followed by x-ray pictures and there appeared to be some correlation between the demonstration of toxin in the blood stream with distention of the loops. Gross necrosis of the distended segments did not always occur where there was absorption, but devitalization of the bowel segments greatly facilitated the appearance of toxin in the blood stream.

# PNEUMOPERITONEUM IN PERFORATIONS OF THE GASTRO-INTESTINAL TRACT

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## INTRODUCTION

SINCE the diagnosis of "acute abdomen" is no longer, in all cases, considered to be indicative of an immediate operation, an ever increasing importance must be placed on the correct diagnosis of acute lesions within the peritoneal cavity. That the usual physical examination by means of inspection, palpation, percussion, and auscultation is insufficient to arrive at a correct diagnosis in many such cases is only too well known to every surgeon who sees these conditions. In cases of frank perforation of a peptic ulcer, the diagnosis is frequently easy, but in many instances of imminent or forme fruste perforations of a duodenal or gastric ulcer, as well as in cases of trauma to the abdomen with perforation of the small intestine or colon, the percentage of wrong diagnoses is quite appreciable. Any practical means of arriving at an exact diagnosis of whether actual perforation has occurred would be of great value in the treatment of this type of disease.

In 1915, Popper<sup>6</sup> first suggested the x-ray visualization of a subphrenic collection of gas with the patient in an upright position as an aid in the diagnosis of perforated peptic ulcers. In the following year, Lenk<sup>7</sup> noticed the occurrence of pneumoperitoneum following bullet wounds of the abdomen and recommended the use of x-ray examination in the diagnosis of perforations of the gastrointestinal tract. Dandy,<sup>2</sup> in 1919, noted a subphrenic pneumoperitoneum on the chest plate of a patient with a perforated ulcer of the transverse colon. This chance observation later led to the development of ventriculography. Vaughan and Brams<sup>13</sup> in 1925 published the first series of cases of any size in which this method of diagnosis was used. They found that subphrenic accumulations of gas could be demonstrated in 86.2 per cent of 29 proved cases of acute perforation of peptic ulcers. Other series have been reported as follows:

Vaughan and Singer (1929):<sup>14</sup> 63 proved cases of perforated peptic ulcer; 54 cases showed presence of pneumoperitoneum on x-ray examination—87 per cent.

Finsterbusch and Gross (1932):<sup>3</sup> 110 proved cases of perforated peptic ulcer collected from the literature; 95 cases showed presence of gas by x-ray examination—86 per cent.

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2. This toxin injected intraperitoneally, in suitable doses, is readily absorbed into the blood stream. The toxin may be demonstrated in the blood within two hours; it increases in quantity with time, and is lethal to the dog.

3. Absorption of *Cl. botulinum* toxin placed in small quantities in obstructed segments of the small intestine of dogs has been demonstrated. The distention of the isolated loops was followed by x-ray pictures and there appeared to be some correlation between the demonstration of toxin in the blood stream with distention of the loops. Gross necrosis of the distended segments did not always occur where there was absorption, but devitalization of the bowel segments greatly facilitated the appearance of toxin in the blood stream.

short attacks of epigastric discomfort with pain radiating to the right shoulder. These attacks usually followed meals and lasted ten to fifteen minutes. At no time had she been confined to her bed.<sup>3</sup> Physical examination was essentially negative except for the absence of liver dullness on percussion of the abdomen. Various x-ray films of the abdomen (Fig. 1) showed the presence of a massive pneumoperitoneum. Roentgen examination of the stomach and colon, as well as a cholecystogram, were all negative. Despite the fact that the patient was afebrile and had no acute complaints or evidences of peritonitis, an exploratory laparotomy was advised. This the patient refused and left the hospital nineteen days after admission. A definite cause for the pneumoperitoneum was never determined.

#### EXPERIMENTAL OBSERVATIONS

In an effort to obtain data concerning how much reliance might be safely placed on negative x-ray findings in suspected cases of gastric and intestinal perforations, certain observations were made on thirteen patients incidental to the production of a diagnostic pneumoperitoneum.

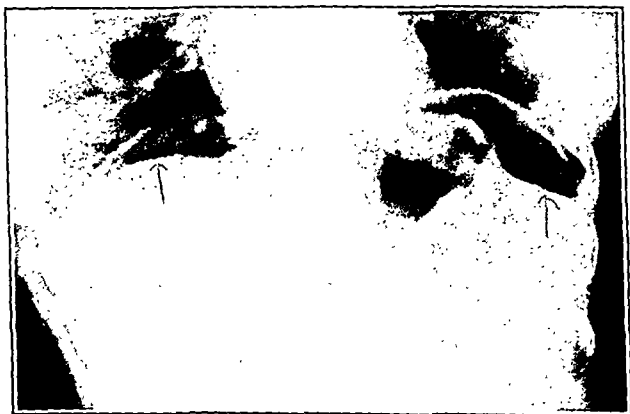


Fig. 1.—Spontaneous pneumoperitoneum, cause undetermined. Roentgenogram of abdomen, upright position, showing gas accumulated (arrows) under each diaphragm. The shadow of the gas-filled stomach and colon and the density of the spleen can be seen on the left side. This appearance is characteristic of pneumoperitoneum whether spontaneous or artificial. In this case no cause for the pneumoperitoneum could be ascertained and there was no evidence of peritonitis.

Similar observations were made on five cadavers shortly after death. These experimental observations were begun at the suggestion of O. H. Wangenstein and had as their purpose the determination, if possible, of how small a quantity of gas could be seen regularly under the diaphragm and, in particular, under the right dome of the diaphragm.

It seems strange that this important point has not been determined before, but the only references to it in the literature are the statement by Vaughan and Brams in 1925<sup>13</sup> that only a few cubic centimeters of air were required to be seen by the x-ray method, and the statement by Friedman in 1934<sup>4</sup> that no definite determination had been made as to the smallest amount of gas that would cast a shadow, but that it was believed that as little as 50 c.c. might be visualized on an x-ray film.



Spinzig (1933):<sup>11</sup> 21 proved cases of perforation of the gastrointestinal tract; 21 cases showed the presence of gas by x-ray examination—100 per cent.

Johnson (1937):<sup>6</sup> 42 proved cases of perforated gastric and duodenal ulcers; 35 cases showed the presence of gas by x-ray examination—83 per cent.

Petrén (1937):<sup>8</sup> 40 proved cases of perforated gastric, duodenal, and gastro-jejunal ulcers; 27 showed the presence of gas by x-ray examination—68 per cent.

#### CRITERIA OF PERFORATION

The criteria by which writers have considered free perforations to be proved have been, in practically all cases, the demonstration at operation or autopsy of a perforation in free communication with the general peritoneal cavity, or the demonstration of a pneumoperitoneum by x-ray. A moment's consideration will show that figures drawn from a series of cases based on the above criteria must be somewhat weighted in favor of the accuracy of x-ray diagnosis, since no account is taken of those cases of perforation, such as the sealed or forme fruste type which shows no gas by x-ray examination, which is not operated upon, and which is not autopsied. It should be borne in mind further that failure to find a perforation at operation or during the course of a routine autopsy does not absolutely exclude the possibility of its presence. On the other hand, there are certain objections to the acceptance of the presence of a pneumoperitoneum without confirmation at autopsy or operation as proof of a gastrointestinal perforation in the usual sense. The fact that a ruptured appendix might theoretically give rise to a pneumoperitoneum must not be overlooked. While in our experience such a condition has not been detected in a large number of roentgenograms taken for the purpose of determining whether pneumoperitoneum was present in frank cases of perforation of the appendix, isolated case reports do appear in the literature. Cases of so-called "gas peritonitis," in which a peritonitis with the concomitant formation of free gas in the peritoneal cavity is present, have appeared rather frequently in the recent German literature. One such case has been seen at the University of Minnesota Hospitals.

**CASE REPORT.**—A forty-three-year-old Mexican woman presented an acute inflammatory lesion in the abdomen. A large unencapsulated pneumoperitoneum was demonstrated by x-ray examination. Under a diagnosis of perforated peptic ulcer, this patient was operated upon. Careful exploration of the abdomen revealed no sign of a perforation of the gastrointestinal tract nor any source of the generalized peritonitis which was present. The patient died, but autopsy was not permitted. In the absence of a carefully performed autopsy, it must be admitted the possibility of a gastrointestinal perforation was not completely excluded.

Rare cases are seen in which gas is found in the peritoneal cavity without symptoms and without obvious cause. One such instance has been observed at this hospital (Fig. 1).

**CASE REPORT.**—A thirty-one-year-old white woman had complained of vague pain in the lower part of her back for three months. During this time she had several

tients in the left lateral decubitus position; i.e., a posteroanterior projection with the patient lying on the left side.

The results of these observations showed that when small quantities of air (10 c.c.) were injected, all, or portions, of it frequently re-

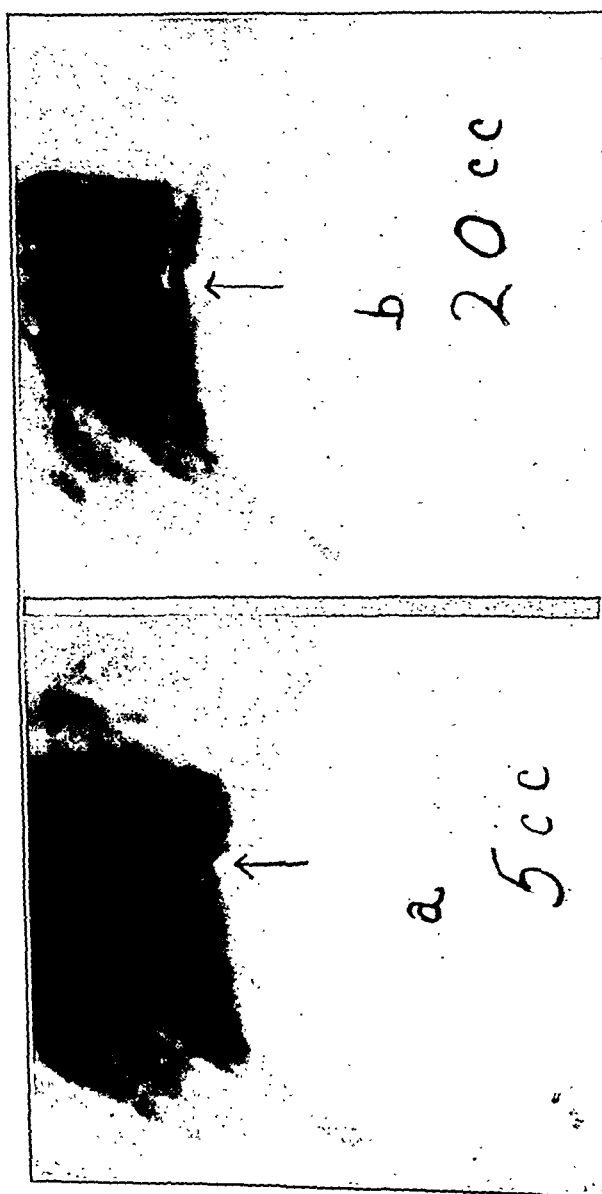


Fig. 3.—A, Experiment on cadaver; roentgenogram after introduction of 5 c.c. of air under the right diaphragm showing clearly the presence of gas. B, Same experiment as A, showing increased visualization of air after injection of 20 c.c.

mained localized for a short time at the site of injection. Usually after a few seconds, particularly if the abdomen was massaged or if the patient took several deep breaths, this gas tended to accumulate beneath the diaphragm. In the average case 20 to 30 c.c. of air had

A. *Observations Incidental to Diagnostic Pneumoperitoneum.*—In thirteen patients with abdominal lesions, pneumoperitoneum was produced for purposes of diagnosis. The gas injected was either air, oxygen, or carbon dioxide. Carbon dioxide was used in the majority of the cases as it was found that quantities of this gas as large as 1,600 c.c. were almost completely absorbed from the peritoneal cavity within a few hours. During this time the desired x-ray films could be made and the discomfort which the injection of gas occasionally produced was diminished to a minimum. However, in the preliminary experimental observations made on these patients and reported here, air was used as the injected medium to obviate the rapid absorption of carbon dioxide.\*



Fig. 2.—Artificial pneumoperitoneum. Roentgenogram of abdomen in upright position demonstrating outline of liver, gallbladder, spleen, and adhesions. Note complete absence of gas under right diaphragm, between left lobe of liver and left diaphragm, and between spleen and left diaphragm. There appears to be a small segment of left diaphragm under which the gas has accumulated. Due to adhesions even the large amount of air injected does not accumulate in the subphrenic spaces.

The abdominal wall, at a point slightly below the umbilicus and about two inches to one side of the midline, was infiltrated with 1 per cent novocaine. The patient was then placed on the fluoroscopic table in the vertical position and small measured quantities of air were injected into the peritoneal cavity by means of a needle inserted through the anesthetized area. During the time of the injection and at frequent intervals immediately afterwards, the site of injection and the subdiaphragmatic areas were observed through the fluoroscope. Similar injections and observations were also made with some of the pa-

\*Other observations have shown that 1,200 to 1,600 c.c. of carbon dioxide are completely absorbed from the peritoneal cavity in twenty-four hours. Similar quantities of oxygen are absorbed within four to seven days. The same amount of air, as demonstrated by x-ray examination, will not be completely absorbed for as long as two weeks after injection.

position is of very great value under such conditions as gas can thus be demonstrated between the lateral abdominal wall and the liver even if the subphrenic space is sealed.

*B. Observations Made on Cadavers.*—The above observations indicated that small amounts of air injected into the peritoneal cavity of the average patient at a point some distance from the diaphragm probably did not reach the subphrenic spaces immediately or in their entirety. The following experiments were therefore performed on five cadavers within two hours after death.

The cadaver was first strapped to the fluoroscopic table and then placed in the vertical position. A small portion of the ninth or tenth



Fig. 5.—Same case as shown in Fig. 4. Posteroanterior roentgenogram in left lateral decubitus position showing shifting of gas which occupies the space between the lateral abdominal wall, the diaphragm, and the liver. The fluid level has also shifted so that it is parallel to the long axis of the body.

rib in the midaxillary line on the right side was resected, and by means of a syringe and hypodermic needle, varying quantities of air were injected through the diaphragm directly into the subphrenic space. As soon as any suggestion of air between the diaphragm and upper surface of the liver could be seen with the fluoroscope, an x-ray film was exposed on the fluoroscopic table.

In two of the cadavers 5 c.c. of air was clearly visualized (Fig. 3a), and in all five cadavers 10 c.c. was readily seen without any difficulty (Fig. 3b). Similar observations made with the cadaver in the left lateral position indicated that somewhat larger amounts of air (10 to 20 c.c.) had to be injected to be seen regularly.

to be injected before an unmistakable subphrenic accumulation could be seen. In the occasional case quantities of air as large as 50 c.c. had to be used and in these cases the place where it was often seen first was lateral to the right lobe of the liver instead of above it. It was our impression that air tended to accumulate more frequently and in larger amounts under the right dome of the diaphragm than under the left. In any event, a small quantity of air was more frequently and more quickly observed under the right dome than under the left. In one case, despite the establishment of a large diagnostic pneumo-

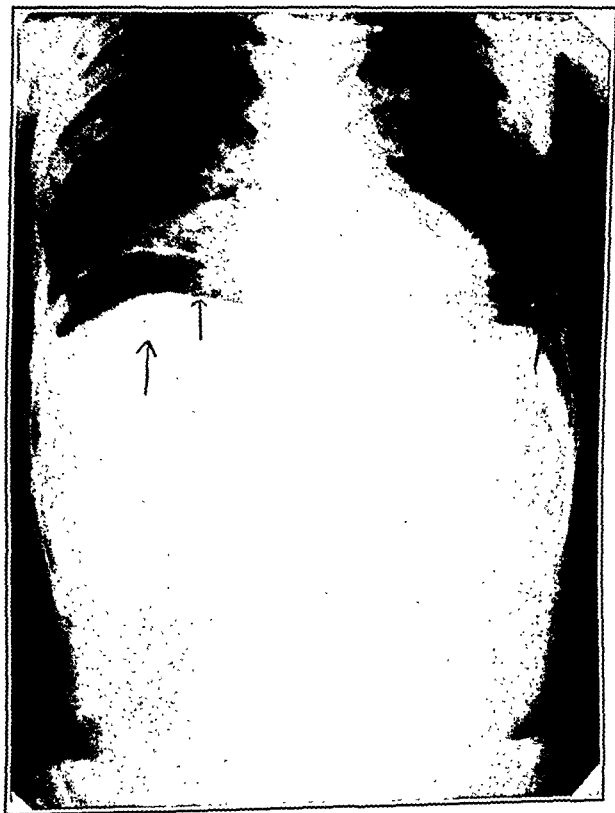


Fig. 4.—Spontaneous perforation of duodenal ulcer. Roentgenogram of abdomen in upright position showing characteristic accumulation of gas under both diaphragms. The presence of fluid in the peritoneal cavity is also shown by the dense horizontal shadow beneath the gas, i. e., the fluid level.

peritoneum of 1,400 c.c. of carbon dioxide, no gas ever appeared under the right diaphragm and only a small portion under the left (Fig. 2). At that time, this observation was interpreted as indicating extensive adhesions between the under surface of the diaphragm and the liver and spleen. A subsequent laparotomy demonstrated the presence of an extensive tuberculous peritonitis. It is obvious that in cases of this type examination in the upright position, as usually done, would fail entirely to reveal gas. Examination in the left lateral decubitus

which had occurred five hours before the x-ray examination was made. The x-ray films taken in the other case were poor exposures, but we are unable to say whether failure to demonstrate a pneumoperitoneum was dependent on this poor technique or some other factor. With small quantities of gas, films of poor quality may readily prevent a correct diagnosis.

In the 6 cases in which a pneumoperitoneum was demonstrated by x-ray study, gas was seen under both sides of the diaphragm in every instance (Fig. 6). Roentgen examination was made with the patient in the left lateral decubitus position in only two instances. (Fig. 7.)

*B. Perforations of the Duodenum.*—Thirty cases out of a total of 37 proved cases of perforation of the duodenum at the site of duodenal ulcers were submitted to x-ray examination. Free gas in the peritoneal cavity could be demonstrated in only 22 instances, or 73.3 per cent. An x-ray film with the patient in the vertical position was made in each of the 22 cases (Fig. 5). A film with the patient in the left lateral decubitus position as well as the vertical position was made in only 14 instances (Fig. 6). In 3 cases free gas could be seen on the upright plate, but not on the decubitus film. In 1 case free gas could be seen on the decubitus film, but not on the upright. Of the 21 cases in which a free subphrenic pneumoperitoneum was present in the upright film, it was present under the domes of both diaphragms in 10 instances; under the right dome but not the left, in 9 instances; and under the left dome but not the right, in 2 instances (Fig. 8).

One of the 8 proved cases of perforation of the duodenum which did not show the presence of free gas in the peritoneal cavity by x-ray examination was an extremely obese moribund patient in which the x-ray films were not clear enough to be read satisfactorily. Failures in diagnosis due to such a cause have been included in our series, since for practical purposes they constitute a valid objection to the use of the x-ray method of diagnosis.

No adequate explanation of the failure to visualize gas by x-ray examination in the other 7 cases of duodenal perforation is apparent. All were perforations of duodenal ulcers in the anterior wall of the first or second portions of the duodenum. The average size of the perforation was 5 mm. The average time interval between perforation and x-ray examination was five and one-half hours.

*C. Perforations of the Small Intestine.*—A diagnosis of perforation of the jejunum or ileum was made in 4 instances. Each of these perforations was demonstrated at either operation or autopsy examination. Two of these 4 cases were submitted to x-ray examination. One was a perforation of a tuberculous ulcer in the distal portion of the ileum. This case was seen at the hospital and x-ray examination made sixteen hours after the perforation had probably occurred. Free

## TECHNIQUE OF X-RAY EXAMINATION IN CLINICAL CASES

Many of the clinical cases to be reported here were examined only in the upright position, some with fluoroscopic observation, others by posteroanterior roentgenograms alone. Whenever possible the films were made at the end of deep inspiration. In the past few years three exposures have been made; one a posteroanterior with the patient upright (Fig. 4), one an anteroposterior with the patient supine, and one a posteroanterior with the patient lying directly on the left side with the right side up (Fig. 5). In the past year these films have been made with the Potter-Bucky diaphragm; prior to that they were made without it.

## ANALYSIS OF CLINICAL CASES

At the University of Minnesota Hospitals a diagnosis of perforation of the stomach, duodenum, jejunum, ileum, or colon was made in 70 instances during the ten-year period, 1927 to 1937. Forty-seven of these 70 cases were submitted to x-ray examination to determine the presence or absence of a subphrenic pneumoperitoneum. In 56 of these 70 patients the presence of a perforation was demonstrated at either operation or autopsy. In 6 other cases the actual proof of perforation was dependent upon the demonstration of a pneumoperitoneum by x-ray examination. In the remaining 8 cases the diagnosis of perforation was based on the clinical findings and physical examination alone. These 70 perforations were divided with respect to anatomic location as follows:

ANATOMIC LOCATION OF PERFORATIONS OF GASTROINTESTINAL TRACT: UNIVERSITY OF MINNESOTA HOSPITALS, 1927-1937

		DIAGNOSIS CONFIRMED BY:		
		OPERATION OR AUTOPSY	X-RAY EXAMINATION ALONE	HISTORY AND PHYSICAL EXAM- INATION ALONE
Stomach	14	11	1	2
Duodenum	43	33	4	6
Small intestine	4	4	-	-
Colon	9	8	1	-
		56	6	
Total	70		62	8

*A. Perforations of the Stomach.*—In the 14 instances of perforation of the stomach, 12 peptic ulcers, and 2 carcinomas, definite proof of perforation was obtained in 12. Only 8 of these cases, however, were submitted to x-ray examination and in 6 cases only was free gas demonstrated in the peritoneal cavity. In other words, the x-ray diagnosis of perforation was only 75 per cent correct in this small series of cases. One of the 2 proved cases of perforation in which x-ray examination failed to demonstrate a free pneumoperitoneum was a 4 mm. perforation on the anterior surface of the pyloric portion of the stomach

gas was seen under both domes of the diaphragm in a roentgenogram taken with the patient in the upright position. The other case was that of a boy with a perforation of the jejunum. The first examination, eight hours after the perforation, failed to show any signs of a pneumoperitoneum. A second roentgen examination, sixteen hours later, showed the presence of gas beneath the left dome of the diaphragm.

The results of the x-ray examination in these 2 cases agree well with our clinical impression that in early perforations of the small intestine roentgenography is of much less value in diagnosis than in those cases where a considerable interval has elapsed between the perforation and the x-ray examination.

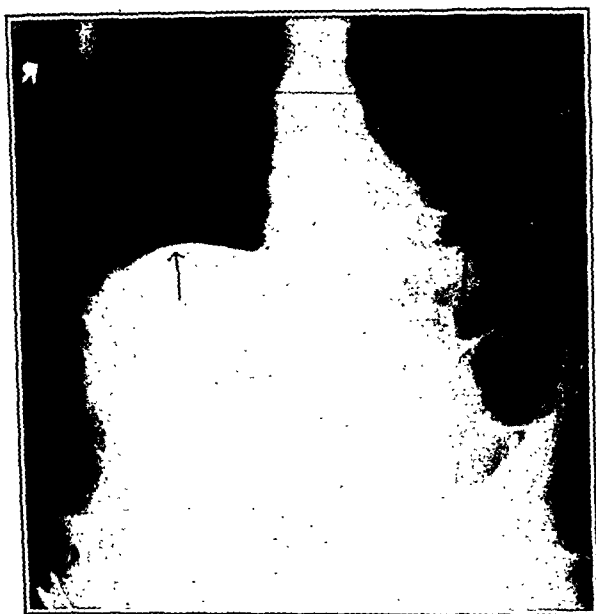


Fig. 8.—Perforation of duodenal ulcer. Roentgenogram of abdomen in upright position showing a large amount of gas under the left diaphragm, while none can be seen on the right side. The confusing shadows on the left side caused by the gas in the stomach and colon are apparent.

*D. Perforations of the Colon.*—The experience of any large hospital attests the fact that the most common cause of perforation of the colon is obstruction of that organ. This is brought about by the fact that in the great majority of patients the ileocecal sphincter and valve effectually precludes the retrograde passage of feces and gas which gain entrance to the colon or are produced there. An increasing intracolonic pressure, such as occurs in obstruction, will in time produce necrosis and rupture of the cecum by stopping the flow of blood through the vessels in its walls. Thus the mechanism and clinical course of perforations of the colon are different from the usual mechanism and clinical course of perforations of the stomach and





Fig. 6.—Spontaneous perforation of gastric ulcer. Roentgenogram of abdomen in upright position showing moderate accumulation of gas under the left diaphragm (arrow). The gas and fluid in the cardia of the stomach are shown below the shadow of the gas. On the right there is a much smaller amount of gas (arrow) which does not spread through the whole subphrenic space.



Fig. 7.—Same case as shown in Fig. 6. Posteroanterior roentgenogram in left lateral decubitus position showing shifting of gas under right diaphragm to a more caudad position (arrow). It should be noted that the shadow of the gas on the right side is more obvious in this film than in the one made with the patient upright.

With very small quantities of gas, however, after it has reached the subphrenic space, the shadow may be obscured by the dome of the liver on the right side or a distended stomach on the left unless the x-rays are directed in a fairly exact vertical direction with respect to the longitudinal axis of the body and unless the longitudinal axis of the body is vertical with the floor at the time the x-ray examination is made. This is purely a question of gravity. Technical difficulties due to unusually large patients, inability of the patient to cooperate in stopping respiratory movements, technical errors which are prone to occur in cases which are examined under emergency conditions, all tend to militate against clear visualization of the faint shadow produced by small quantities of gas.

Those factors, however, which operate to prevent the escape of gas through a perforation are probably of more significance in decreasing the accuracy of x-ray diagnosis. The influence which the concomitant presence of both fluid and gas in a viscus at the time of perforation plays in the escape of gas from that viscus would seem quite appreciable if the site of perforation should happen to be located below the fluid level. Unless the patient assumes a supine or left lateral position following a perforation of the stomach or duodenum, a considerable quantity of fluid may escape before any gas can gain access to the free peritoneal cavity. Occasionally food particles or plugs of mucus become caught in the perforation and serve as an adequate seal until the reaction of the surrounding peritoneum and omentum has effectively localized or walled off the perforation. In some instances the redundant mucosa of the stomach and small intestine may prolapse through the perforation and prevent the escape of gas for a variable period of time. Recent experimental work by Bergh, Bowers, and Wangenstein<sup>1</sup> on the factors influencing the development of peritonitis in perforations of the gastrointestinal tract of dogs has a direct bearing on this question.

#### THE VALUE OF ROENTGEN EXAMINATION IN THE LEFT LATERAL DECUBITUS POSITION

X-ray examinations of 14 patients with perforation of the duodenum were made with the patient in both the upright and left lateral decubitus positions (Figs. 5 and 7). In no other type of perforation have enough examinations in the left lateral decubitus position been made to furnish a basis for appraisal of this procedure from a diagnostic standpoint. In 3 patients a pneumoperitoneum was seen in the upright position, but not in the lateral position, and in only 1 patient did the examination in the lateral position permit a diagnosis when the upright failed.

The left lateral decubitus position, however, has several advantages. In the occasional case in which the subphrenic space is obliterated by

duodenum. We have included them, however, for the sake of completeness. Nine cases of perforation of the colon have been observed. Eight of these perforations have been verified by operation or postmortem examination. Proof of perforation in the remaining case rests on the visualization of a free pneumoperitoneum on an x-ray film. An x-ray examination was made in 7 of these 9 cases of perforation and free pneumoperitoneum was seen in all of them. The cause of perforation was carcinoma of the colon with obstruction in 5 cases; obstruction of the sigmoid flexure in a strangulated left indirect inguinal hernia, in 1 case; rupture of the uterus which was adherent to the sigmoid flexure, in 1 case; perforation of an ulcer of the colon, the etiology of which was not determined, in 1 case; and the accidental perforation of the wall of the colon with a suture in the closure of a laparotomy incision, in 1 case.

None of the 7 cases of perforation of the colon which were submitted to x-ray examination were early perforations. The time interval between perforation and x-ray examination was over twenty-four hours in every case and as long as several days in some cases. Four of these 7 perforations occurred in the presence of obstruction of the colon. These two factors, i.e., a lapse of at least twenty-four hours between perforation and x-ray examination and the presence of obstruction with the concomitant large accumulation of gas in the colon at the time of perforation, may explain the fact that roentgenography was 100 per cent correct in the diagnosis of these lesions. It is quite doubtful that an equal degree of accuracy is attained by roentgen examination in early cases of colonic perforation or in cases occurring in the absence of colonic obstruction.

#### FACTORS TENDING TO DECREASE THE ACCURACY OF X-RAY DIAGNOSIS IN PERFORATIONS OF THE GASTROINTESTINAL TRACT

One may well ask that if such small quantities of gas as 5 to 10 c.c. can be consistently seen in the subphrenic space on an x-ray film, why is not the accuracy of diagnosis by x-ray examination in cases of intra-abdominal perforation of the gastrointestinal tract even greater than the usually reported 85 per cent. The answer to this question cannot be stated with certainty, but several factors seem to merit consideration.

If one assumes that a very small quantity of gas has escaped from the stomach or intestine, it will reach the subphrenic space in a short time, provided the space has not been obliterated by adhesions and provided the patient assumes at least a semierect position for two or three minutes before the x-ray examination is made. Rubin<sup>10</sup> has stated that, in the living patient, when an artificial pneumoperitoneum has been created gas collects under the right diaphragm in two or three minutes. Geier<sup>5</sup> has reported a case of perforation of a gastric ulcer in which gas was seen under the diaphragm ten minutes following the perforation.

With very small quantities of gas, however, after it has reached the subphrenic space, the shadow may be obscured by the dome of the liver on the right side or a distended stomach on the left unless the x-rays are directed in a fairly exact vertical direction with respect to the longitudinal axis of the body and unless the longitudinal axis of the body is vertical with the floor at the time the x-ray examination is made. This is purely a question of gravity. Technical difficulties due to unusually large patients, inability of the patient to cooperate in stopping respiratory movements, technical errors which are prone to occur in cases which are examined under emergency conditions, all tend to militate against clear visualization of the faint shadow produced by small quantities of gas.

Those factors, however, which operate to prevent the escape of gas through a perforation are probably of more significance in decreasing the accuracy of x-ray diagnosis. The influence which the concomitant presence of both fluid and gas in a viscus at the time of perforation plays in the escape of gas from that viscus would seem quite appreciable if the site of perforation should happen to be located below the fluid level. Unless the patient assumes a supine or left lateral position following a perforation of the stomach or duodenum, a considerable quantity of fluid may escape before any gas can gain access to the free peritoneal cavity. Occasionally food particles or plugs of mucus become caught in the perforation and serve as an adequate seal until the reaction of the surrounding peritoneum and omentum has effectively localized or walled off the perforation. In some instances the redundant mucosa of the stomach and small intestine may prolapse through the perforation and prevent the escape of gas for a variable period of time. Recent experimental work by Bergh, Bowers, and Wangenstein<sup>1</sup> on the factors influencing the development of peritonitis in perforations of the gastrointestinal tract of dogs has a direct bearing on this question.

#### THE VALUE OF ROENTGEN EXAMINATION IN THE LEFT LATERAL DECUBITUS POSITION

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adhesions, a collection of gas may be seen which otherwise would be missed. The chief criticism of the x-ray method of diagnosing gastrointestinal perforations has been that it was too strenuous a procedure for critically ill patients. While this criticism may or may not have merit as regards this examination in the upright position, certainly little criticism can be made of the use of the lateral decubitus exposure. The patient need not be moved or raised from his bed or litter. All that is required is that he lie on his left side.

The added information gained from the film made in this position, when taken together with the upright, is often valuable in deciding

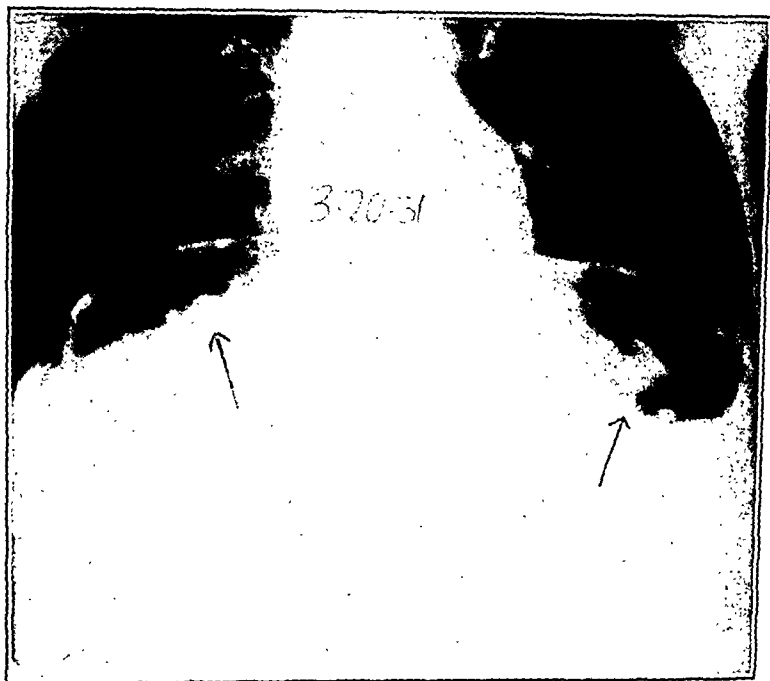


Fig. 9.—Ptosis of the liver and distention of the colon. Roentgenogram of diaphragmatic regions in upright position showing marked accumulations of gas in stomach and splenic flexure of colon (arrow) under left diaphragm. On the right side the liver has been displaced downward by the distended hepatic flexure which simulates the appearance of free gas in the subphrenic space. Note the irregular segmented character of the gas shadow under the right diaphragm which denotes that the gas is within the colon.

whether an accumulation of gas seen under the diaphragm is free in the peritoneal cavity or localized in an abscess (Figs. 4-7). We feel that a gaseous shadow which shifts with change in the patient's position is confirmatory evidence on this point. Collections of gas contained within the stomach or bowel may on occasion cause some doubt as to the diagnosis of a free pneumoperitoneum. This is particularly true in those cases where the pneumoperitoneum is confined to the left subphrenic space. In such cases a stomach distended with gas frequently obscures the pneumoperitoneum and presents a very

confusing picture (Figs. 8 and 9). X-ray films made with the patient in the right lateral decubitus position may be of help in these cases, but they are often of no value because of the multiple gaseous shadows frequently produced in the left upper quadrant by the colon and small intestine. Under such circumstances it has been the practice at the University Hospitals to empty the stomach through a nasal catheter and then reexamine the patient in the upright position. This simple procedure usually suffices to settle this question.

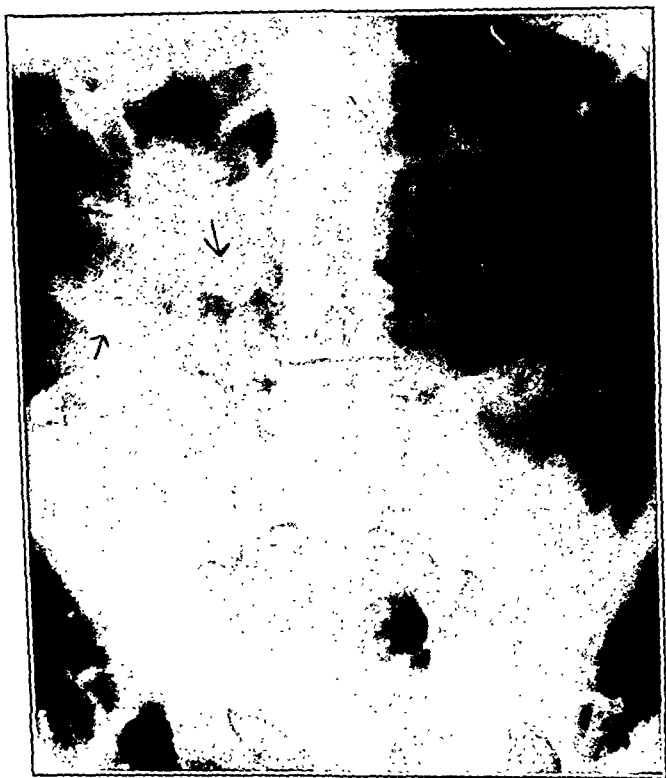


Fig. 10.—Acute obstruction of sigmoid colon from hernia with secondary rupture of cecum and pneumoperitoneum. Roentgenogram of abdomen in supine position showing marked distention of bowel with gas. Note that outer walls of intestine are clearly visible, indicating presence of free gas in peritoneal cavity without the use of upright or lateral decubitus positions.

In rare instances when the liver is ptotic, the hepatic flexure of the colon may be seen occupying the right subphrenic space (Fig. 9). Unless this is kept in mind and the characteristic signs of gaseous accumulations in the colon observed, an erroneous diagnosis of subphrenic pneumoperitoneum may occasionally be made. The fact that air will often remain in the peritoneal cavity for several weeks after laparotomy must also be borne in mind so that a mistaken diagnosis of perforation may not be made in such cases.



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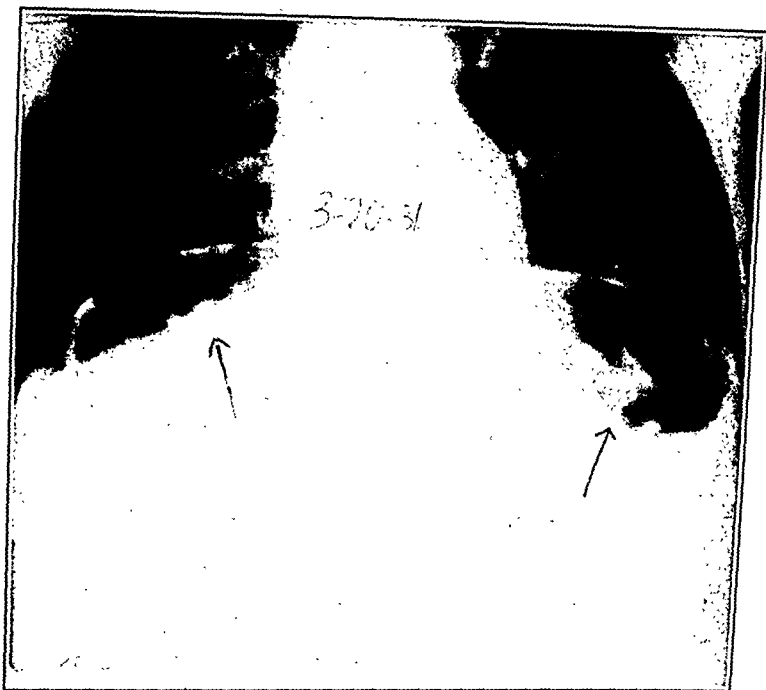


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or duodenum. Our experience with such cases wholly substantiates the soundness of the conservatism advocated by Vaughan and Singer in such instances.

*B. Suspected Perforations of Small Intestine and Colon.*—That the evidence of roentgenography in perforation (usually traumatic) of the small intestine or of the colon (usually due to tension perforation consequent upon a carcinomatous block) is even less reliable than in perforation of the stomach or duodenum is the common experience of those who have used this agent widely for the detection of such lesions. Wangenstein<sup>16</sup> has called attention to the shortcomings of the roentgen films for this purpose in suspected traumatic perforation of the intestine by nonperforating types of injury. This impression is opposed to the actual experience as recorded in this paper, but the number of cases here reported is small. Proof of the reliability of x-ray evidence for early demonstration of perforation of the small intestine or colon is still wanting and is demanding of further elaboration. The policy in this clinic is to subject suspected and demonstrated perforations to early operation, at which time the perforation is sought out and closed.

#### SUMMARY

Any means of making an exact diagnosis as to whether perforation of the stomach, intestine, or colon had occurred would be a boon to surgeons treating these conditions and would lower the incidence of operations now performed for acute abdominal conditions.

The use of the x-ray demonstration of subphrenic pneumoperitoneum as an aid in making such diagnoses has been recommended by various men since 1915. The accuracy of the diagnoses made in this way has varied from 68 to 100 per cent in the various series reported. It is probable that the actual percentage is somewhat lower.

By experiments on 5 cadavers it has been shown that at times as small a quantity of gas as 5 c.c., in the right subphrenic space, can be demonstrated on an x-ray film. Ten cubic centimeters can be seen regularly without difficulty.

There have been 62 proved cases of perforation of the stomach, duodenum, small intestine, and colon treated at the University of Minnesota Hospitals between 1927 and 1937. Forty-seven of these cases were submitted to x-ray examination and gas outside the gastrointestinal tract was observed in 78.8 per cent of them. In 38 cases of perforation of the stomach or duodenum, free gas was observed in 28 (73.7 per cent).

The reasons why gas is not seen in every case probably include the following:

1. Adhesions in the right upper quadrant of the abdomen.
2. Location of the perforation below the fluid level of the fluid in the viscus.

In an occasional case, examination must be restricted to films made with the patient in the supine position. Under these circumstances diagnosis is rendered more difficult, but it is well to bear in mind that moderate quantities of gas in the peritoneal cavity will outline the hollow viscera which are usually distended with gas themselves (Fig. 10). Under such conditions the thickness of the wall of the stomach or bowel may be clearly visible, both the inner surface and the serosal surface being delineated by the gas. This may give the clue to the presence of air previously unsuspected.

#### INDICATIONS FOR OPERATION

*A. Perforations of the Stomach and Duodenum.*—The practice in this clinic is to operate upon all cases of demonstrated perforation except those in which reliable evidence of encapsulation is present. Even late cases without encapsulation are best treated by efforts directed at closure of the perforation. The question of operation in those cases in which pneumoperitoneum is not demonstrated by x-ray or in which it appears to be encapsulated must be decided on the basis of history and physical findings of each case.

All cases in which pneumoperitoneum can be demonstrated in which the history indicates a recent onset should be considered as open leaks into the general peritoneal cavity. In those instances in which some time has intervened (forty-eight hours or more) and the patient's status (especially the pulse) seems satisfactory despite a large pneumoperitoneum, encapsulation may be considered as having occurred. Such a patient warrants conservative treatment. Wangenstein<sup>15</sup> has described such instances and discussed their management by conservative means. Vaughan and Singer<sup>14</sup> have advocated the nonoperative treatment of instances of so-called sealed perforations in which the clinical picture is that of ulcer perforation, but in which no gas can be visualized below the diaphragm on a properly exposed x-ray film. Similar cases have been described by Wangenstein; and in this clinic, in the instances in which the clinical picture of ulcer perforation was present and in which conservative treatment was carried out (suction applied to an inlying duodenal tube, paraoral fluids, hot packs, and subsequent check-up roentgenograms), no patient has come to grief. Our experience, therefore, has been that this practice has been safe. Yet 9 cases (7 perforations of the duodenum and 2 perforations of the stomach), in which an unsealed perforation was found at operation despite negative x-ray evidence, throw legitimate doubt upon the validity of that conservatism. Vaughan and Singer have also described the conservative management of the forme fruste type of perforation, i.e., the patient with the very small pneumoperitoneum who comes after the lapse of some time. In such instances sealing probably occurs soon after the escape of a small quantity of gas from the stomach

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3. Absence of gas in the viscus at the time of perforation.
4. Temporary plugging of the perforation with stomach or intestinal content until the perforation is walled off.
5. Prolapse of redundant mucosa into the perforation blocking the exit of gas.
6. Technical failures in the roentgen examination in cases wherein small amounts of gas are present. These include failure to direct the x-rays horizontal to the long axis of the body, failure to have the patient in the upright position for a few minutes prior to the examination and vertical during the examination, and the ordinary difficulties of roentgen technique.

Roentgen examination in the left lateral decubitus position was found to be of value in establishing the diagnosis of spontaneous pneumoperitoneum. This position is useful when the patient cannot be placed upright. However, if pneumoperitoneum is observed at all on the x-ray film, it will be seen between the right dome of the diaphragm and the liver in 90 per cent of the cases.

Roentgen examination of 2 cases of traumatic perforation of the small intestine showed the presence of free gas in the peritoneal cavity; in one case sixteen hours after perforation, in the other only after twenty-four hours.

#### CONCLUSIONS

1. As little as 5 c.c. of gas in the right subphrenic space can, at times, be demonstrated by roentgen examination under experimental conditions.

2. In cases of perforation of the stomach and duodenum failure to demonstrate gas by roentgen examination may occur in over 25 per cent of the cases.

3. In cases of perforation of the small intestine or colon, if the time interval between perforation and examination is long (sixteen hours or more), or if obstruction is present, a subphrenic pneumoperitoneum is consistently observed by roentgen examination.

4. It is recommended that cases of suspected as well as demonstrated perforation of the gastrointestinal tract, except those in which there is definite evidence of encapsulation, be submitted to early operation.

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# PEPTIC ULCERS FOLLOWING EXPERIMENTALLY PRODUCED OBSTRUCTIVE JAUNDICE

A CONSIDERATION OF THE FACTORS CONCERNED IN THEIR PRODUCTION\*

WARREN H. HEBERT, M.D.,† ROCHESTER, MINN.

(From the Mayo Foundation)

MANY OBSERVERS have demonstrated the presence of duodenal ulcers following experimentally produced obstructive jaundice (Kapsinow, Berg and Jobling, Loewy, Bollman and Mann), and others have shown that duodenal ulcers develop following various procedures for the exclusion of bile, either by itself or together with the other duodenal secretions from the duodenum (Exalto, Mann and Williamson, Morton, McCann, Neuman, Demoor, and Deloyers, Matthews and Dragstedt, Mann and Bollman,<sup>10</sup> Weiss and Hubster). The factors involved in the production of peptic ulcer following obstructive jaundice are obscure. Except for an occasional report in the earlier literature there are few references to gastric secretion in the condition of obstructive jaundice. The records are only briefly reviewed and consist for the most part of observations on cholelithiasis and other diseases of the biliary tract. Hyperacidity, hypoacidity, and anacidity have been found on examination of icteric patients. The few investigators who have been interested in this subject have reported conflicting data; the majority of them, however, are of the opinion that hyperacidity accompanies jaundice in animals.

The theories advanced as to the etiology of peptic ulcer have been summarized recently by McCann, and since the work of Exalto and of Mann and Williamson, many investigators have corroborated the results of their observations on the occurrence of peptic ulcer following exclusion of the duodenal content from the site of emergence of the gastric content. These investigations emphasize the significance of the acidity of the unneutralized chyme in the production of chronic peptic ulcers.

In normal animals it is known that the ulcer-bearing area of the duodenum is subject to a wide range of pH: "It is the site where the onrushes of acidity produced in the normal fundus are met, diluted, neutralized and buffered for acceptance by the intestines."<sup>8</sup> Normal function of this portion of the duodenum depends on the maintenance of an acid-alkali equilibrium. A shift in this equilibrium may result from any one of many factors, and an unbalance may be temporarily or permanently produced in obstructive jaundice. If the buffering

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capacity of the duodenum is diminished without the occurrence of a similar diminution of acidity in the acid chyme, such conditions would appear to be favorable for the formation of ulcer.

The purpose of this study was to determine whether the factors which are known to be of significance in the experimental production of ulcer are operative in the presence of obstructive jaundice and, if so, if they could play a part in the formation of ulcer. My attention was directed primarily to a study of gastric secretion and motility; secondarily, to a determination of the buffering capacity of the content of the isolated duodenum, *in vivo* and *in vitro*, following exclusion of bile by ligation of the common bile duct.

A carefully controlled experimental study of gastric secretion and gastric motility before and after ligation of the common bile duct was made by Still and Carlson. Desiccated bile was first taken up in physiologic saline solution, warmed to body temperature, and injected intravenously in amounts varying between 0.125 and 0.5 c.c. per kilogram of body weight. These investigators found that the immediate effect of this intravenous injection of bile was to lower gastric acidity. In only one dog was there a return to normal values of acidity during the two-hour period of observation. Following these control observations, the common bile duct was ligated. After obstruction to the biliary outflow, the average acidity of the continuous secretion was increased over that in controls and hyperacid values were obtained following test meals. The authors concluded that chronic obstructive jaundice is followed by a decrease in the volume of gastric secretion and by an increase in the acidity of the gastric juice.

Selesniew made esophageal fistulas and carried out gastrostomy on dogs and studied the gastric secretion before and after ligation of the common bile duct. He noted that, following a forty-eight-hour fast, the stomachs of normal dogs were empty except for insignificant amounts of mucus; the stomachs of jaundiced dogs, however, contained small particles of food with bile-stained mucus. In the presence of biliary obstruction gastric juice was of high acidity. Gastric motility was not affected. By means of various test diets he found the gastric acidity was higher in jaundiced than in normal dogs.

Imes studied the neutralizing capacity of the content of the isolated duodenum of animals in the fasting state and following different test diets. The pH and buffering capacity of the combined secretions in the isolated duodenum remained at a fairly constant level (pH 7.1 to 8.15). He found that 100 c.c. of duodenal content required an average of 60 c.c. of tenth-normal hydrochloric acid, with extremes of 40 to 95 c.c., to reduce acidity to pH 4. Following evulsion of the pancreatic ducts, it required only an average of 36 c.c. to reduce 100 c.c. of duodenal content to a pH of 4.

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The second operation consisted of doubly ligating and sectioning the common bile duct (Fig. 1). Cholecystectomy was also performed at the same time on four of the six animals. An icteric tint to the sclera was usually noted within seventy-eight hours. Estimations of plasma bilirubin and hematocrit readings were checked every eight to ten days. An icteric sclera and skin, clay-colored stools, bilirubinemia, and biliuria were considered as evidence of occlusion of the common bile duct. Ulcers developed in two of the six jaundiced animals, on the twenty-first and fifteenth days, respectively. One animal survived 38 days and the other, 75 days. Ulcers failed to develop in four dogs, which lived 102, 102, 45, and 32 days, respectively.

The results of a series of observations on these animals may be summarized in a few brief statements: There was no appreciable alteration in gastric secretion following ligation of the common bile duct. The acidity and volume of gastric juice secreted, as well as the duration of secretion following the injection of histamine or a test meal of meat, were similar when tested before and at intervals after operation. The animals in which ulcers did develop and those in which they did not were also similar in this respect.

Although the animals reacted similarly to gastric stimulants, it was observed that the small amount of gastric content that could be aspirated from the normal fasting dog was usually neutral in reaction; whereas, jaundiced animals frequently yielded more fluid which was usually strongly acid in reaction.

#### THE EFFECT OF BILIARY OBSTRUCTION ON THE BUFFERING CAPACITY OF THE DUODENUM AND ITS CONTENT

In this experiment three healthy dogs were studied. The duodenum was isolated by a two-stage operation, as described by Stevens. Operations were performed under ether anesthesia with an aseptic technique. The first stage consisted of placing an ileal fistula of the Mann-Bollman type in the first portion of the duodenum, and another fistula at, or just distal to, the duodenojejunal junction. In the second stage, the pylorus was sectioned and the duodenal end was inverted. Gastro-jejunosomy was performed, with an end-to-side anastomosis approximately 30 cm. from the caudal fistula in the duodenum (Fig. 2). This permitted direct emptying of the stomach into the jejunum, eliminating reflux of the gastric content. The duodenal content remained with its alkaline secretions undiluted.

Specimens were obtained from the proximal and distal fistulas of the animal, both when fasting and after various diets, and the ranges of pH were estimated. Following this, 0.5 per cent hydrochloric acid was introduced into the proximal fistula through a small rubber catheter at a fixed rate by the gravity drip method. Specimens were collected

The recent work of Stevens on the buffering capacity of the content of the isolated duodenum *in vivo* should also be mentioned. He noted that the content of the duodenum of a fasting animal, after isolation, was capable of neutralizing from 1.5 to 1.75 c.c. of 0.5 per cent hydrochloric acid per minute over a period of two hours.

#### THE EFFECT OF OBSTRUCTIVE JAUNDICE ON THE SECRETORY FUNCTION OF THE STOMACH

Six healthy, adult, trained dogs were used for this study. Under ether anesthesia and with aseptic technique, gastric and duodenal fistulas of the Mann-Bollman<sup>9</sup> type were made. Following a rest period of about three weeks, routine studies of gastric acidity were made after the technique described by McCann. The subcutaneous injection of 1 mg. of

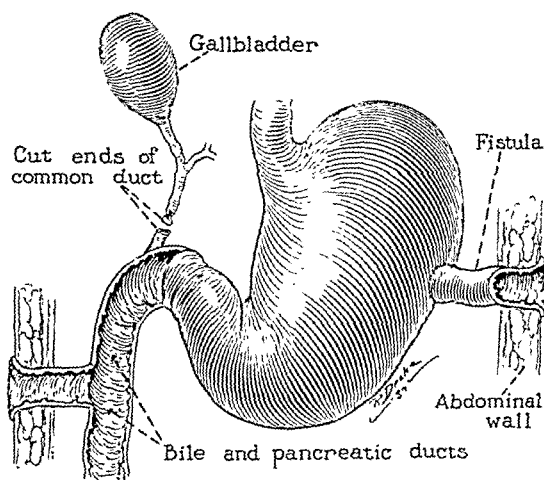


Fig. 1.—Stomach and ileal fistula. The common bile duct has been sectioned and doubly ligated.

histamine and the oral administration of finely diced, lean horse meat were used as stimulants to gastric secretion.

Specimens were collected simultaneously from both fistulas at intervals of fifteen minutes until the gastric acidity and pH had returned to a fasting level. This was accomplished by introducing a soft rubber catheter through each fistula into the stomach and duodenum, respectively. The exact position of the tube in the stomach was determined by roentgenoscopic examination. At each aspiration the entire gastric content was removed and the total volume was estimated. Titration was carried out within a few minutes after each aspiration. The pH was determined by a Leeds-Northrup potentiometer, using the quinhydrone gold electrode. The free and total acidity were determined by titrating clear gastric juice with a solution of tenth-normal sodium hydroxide, using 1 per cent phenolphthalein and 0.5 per cent dimethyl-amino-azobenzene (Töpfer's reagent) as indicators.

Interesting results were noted in the buffering capacity of the duodenal content in vivo and in vitro following the exclusion of bile. In every instance there was a noticeable decrease in the capacity of the duodenum to neutralize acid in the presence of jaundice. The extent of the reduced capacity to neutralize acid after obstruction of the biliary outflow was equivalent to approximately 0.25 c.c. of 0.5 per cent hydrochloric acid per minute for the period of observation.

TABLE I  
BUFFERING CAPACITY OF THE DUODENUM AND ITS CONTENT

DOG	IN VIVO*		IN VITRO	
	C.C. OF 0.5% HCl PER MINUTE		C.C. OF N/10 HCl TO REDUCE pH OF 100 C.C. OF ISOLATED DUODENAL SECRETION TO pH 3.5	
	FASTING	AFTER MEAT MEAL	FASTING	AFTER MEAT MEAL
1	1.25-1.50	1.75	75	85
2	1.00-1.25	1.50	72	88
3	1.50	1.75	77	86

*Following Ligation of Common Bile Duct*

1	1.00		105	
2	0.75-1.00		110	88
3	1.25		92	

*Following Development of Ulcer*

1	0.50	0.50-0.75	80	
2	0.75		70	87

\*The maximal amount of 0.5 per cent hydrochloric acid per minute that may be infused into the duodenum via the proximal fistula without reducing the pH of the fluid from the distal fistula below 7.0.

The neutralizing capacity of the content of the isolated duodenum, in vitro, following obstructive jaundice was increased (Table 1). This was probably because of the fact that the material obtained from the proximal fistula was undiluted with bile and consisted of succus entericus and, for the most part, pancreatic juice.

In the two animals in which gastrojejunal ulcers of the perforating type were present, there were some interesting changes in buffer values. These changes were associated with the development of ulcer and persisted throughout the experiment. In these dogs there was an additional decrease in the buffering capacity of the duodenal juices (succus entericus and pancreatic juice). This amounted approximately to 0.25 to 0.5 c.c. of 0.5 per cent hydrochloric acid per minute for the period during which observations were made. In the absence of ulcer, 105 to 88 c.c. of tenth-normal hydrochloric acid had been necessary to reduce the pH of 100 c.c. of duodenal content to 3.5 to 4. In the presence of a gastrojejunal ulcer, only 80 to 70 c.c. was required to bring about the same alteration of pH. This close parallelism of the figures obtained in vitro and in vivo deserves mention.

from the distal fistula at intervals of fifteen minutes and the pH values were noted. Quantitative determinations of chloride ion were made following introduction of the hydrochloric acid when the animal was fasting and after the various diets.

This procedure was repeated on separate days until the maximal amount of acid that could be introduced into the proximal end of the duodenum without materially changing the reaction of the content of the distal portion was determined. This quantity was considered to be the neutralizing capacity of the normal duodenum and its contents. When

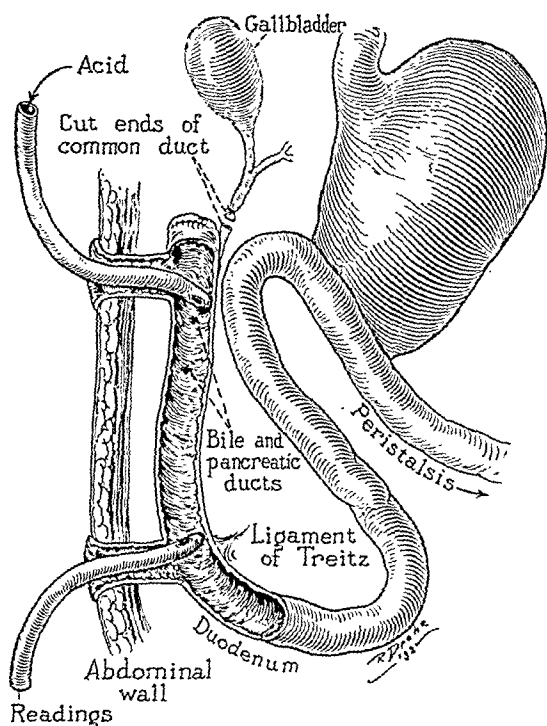


Fig. 2.—A gastrojejunostomy with formation of ileal fistulas; one in the proximal and the other in the distal portion of the duodenum. The common bile duct has been sectioned and doubly ligated.

sufficient data concerning the neutralizing capacity of the duodenum had been obtained, biliary obstruction was produced in each animal by double ligation and section of the common bile duct and the neutralizing capacity of the duodenum was again determined.

Studies of these dogs were resumed on the third to the fifth day after operation. Gastrojejunal ulcers developed in two of the dogs, twenty-eight and thirty-eight days after operation.

The range of pH, as studied from the proximal and distal fistulas of the duodenum in the fasting animals, was approximately the same before and after the exclusion of bile.

Following ligation of the common bile duct, the emptying rate was diminished in three dogs, prolonged in one, and in one no appreciable change was noted. In the three dogs in which emptying was more rapid, an ulcer developed in one.

In the animal in which the average time of emptying of the stomach was prolonged, there were two large duodenal ulcers. It is interesting to note that the change in emptying time was only temporary; the time was eight hours during the second week, three hours during the third week, three hours and one-quarter during the fourth week, and three hours and one-half during the fifth week. Thus, excluding the first emptying rate of eight hours, there was no appreciable change following ligation of the common bile duct.

In the two dogs on which simple cholecystectomy was performed there was no change in the emptying rate of the stomach.

#### SUMMARY

Peptic ulcers occur in a high percentage of dogs in which jaundice is produced experimentally. These ulcers are usually located in the duodenum or appear in the jejunum in animals in which gastrojejunostomy has also been performed. Of the factors which appear to bear some relationship to the formation of the ulcer, the following, which occur after complete biliary occlusion, should be mentioned.

1. The gastric acidity following test meals does not seem to be significantly altered in the jaundiced dog.
2. The acidity and amount of gastric secretion in the fasting stomach is usually found to be increased in the jaundiced dog.
3. The alkalinity of the duodenal content is not materially altered by biliary obstruction.
4. The buffering capacity of the duodenum and its content is definitely reduced after ligation of the common bile duct, and a further diminution occurs when a peptic ulcer is present.

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Determinations were made of the values for chloride in the content of the distal fistula in the fasting state before and following the development of jaundice. The average fasting value for chloride ion was 1.7 mg. per cubic centimeter of duodenal content. After the exclusion of bile, the values were increased to an average of 2.66 mg. per cubic centimeter.

Analyses of gastric content before and after the development of jaundice revealed little if any change. In both animals the gastric acidity was diminished following the development of gastrojejunal ulcer.

#### THE EFFECT OF OBSTRUCTIVE JAUNDICE ON THE EMPTYING TIME OF THE STOMACH

Seven healthy dogs were chosen for the study of the emptying time of the stomach. The general procedure as given below was carried out for a number of weeks for the purpose of training the animals. A test meal of barium was given and the dogs were taken to the fluoroscopic room to accustom them to the darkness and to noises from the roentgen-ray apparatus. By this preliminary preparation they were soon made familiar with a daily routine.

The opaque meal consisted of equal parts of barium sulphate, acacia (10 per cent), and skimmed milk. This barium mixture was administered by mouth without the use of the stomach tube. Examinations were repeated at intervals of four to six days until a fairly constant reading was established for each dog. Roentgenographic examinations were accomplished for the most part without restraint and dogs which had to be gently restrained required the same attention throughout. The stomach was examined within a few minutes following the meal, then hourly for the next two hours, with subsequent observations at intervals of fifteen minutes until the stomach was empty. The average emptying time of the stomach was then determined by repeated observations.

Under ether anesthesia and using an aseptic technique, cholecystectomy, with ligation of the common bile duct, was performed on five of the seven dogs. From the two other dogs the gallbladder was removed and check readings were made to determine any influence on the emptying rate from cholecystectomy alone. At a later date the common bile duct was also ligated in these two animals and further studies were completed.

In the case of the aforementioned five dogs, readings were resumed on the eighth day following operation, with intervals of rest varying from three to six days or more thereafter. Studies were continued as long as the nutritional state and general health of the animals were maintained. The animals were killed for complete examination in 58, 65, 67, 91, and 124 days, respectively. In three animals chronic duodenal ulcers were found.

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# DIFFUSE, CAVERNOUS HEMANGIOMA OF THE RECTUM

## REPORT OF A CASE AND RECORD OF NECROPSY

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THE first known account of hemangiomatous involvement of the rectum was contributed by A. E. J. Barker in 1883. The patient was a man, forty-five years of age, who, when he first consulted Barker in May of 1882, complained of having had periods of rectal bleeding since boyhood. Specular examination of the rectum revealed large folds of mucosa without narrowing of the bowel. There were several shallow, bleeding ulcers, the bases of which presented a mottled, purplish color. The author made a diagnosis of nevoid lipoma of the rectum. The patient failed steadily because of continued loss of blood. At necropsy the wall of the rectum was found much thickened by a "naevoid" growth which gave a purple color to the mucous membrane. The excellent woodcut in Barker's presentation is reproduced here for comparison with our own specimen (Fig. 1).

In Kausch's case, reported in 1916, treatment by posterior excision of the hemangiomatous mass, leaving a permanent stoma, was successful. Examination of the specimen revealed an extensive, cavernous hemangioma of the rectum.

In 1923, Hennig and Schütt reported a case of cavernous lymphangioma of the knee and cavernous hemangioma of the rectum. Necropsy revealed a rectal mucous membrane dark purple in color, inflamed and swollen. The elevation of the "wall" (mucosa?) was caused by thick, spongelike tissue involving the entire thickness of the wall. The microscopic findings conformed to the picture of a typical hemangioma.

In 1923, R. Bensaude and Antoine reported two cases of diffuse, cavernous hemangioma of the rectum. The first was that of a woman, twenty-one years of age, who had had repeated rectal hemorrhages beginning a month and a half after birth. At the age of ten years she was operated on for "hemorrhoids." At the age of fourteen years she underwent first an anal dilatation for fissure, and then an exploratory laparotomy which revealed a large hemangioma of the intestine, passing behind the uterus and disappearing beneath the peritoneum. It had the appearance of a "large bunch of grapes." Nothing curative was done at this time. Pain increased and the patient rapidly became a morphine addict. In 1920, she consulted Antoine, who found her much retarded

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physically and suffering from anemia and amenorrhea. There were frequent rectal hemorrhages. The abdomen was enlarged and tense; there were visible intestinal contractions. Proctoscopic examination for a distance of 30 cm. revealed a marked enlargement of the "anal veins" (external hemorrhoidal veins?). The rectal lumen was obliterated. The mucosa was pale and edematous, but underlying bluish varicosities were seen. When the mucous membrane was swabbed, the cotton applicators became stained with blood, but no bleeding points or ulceration could be

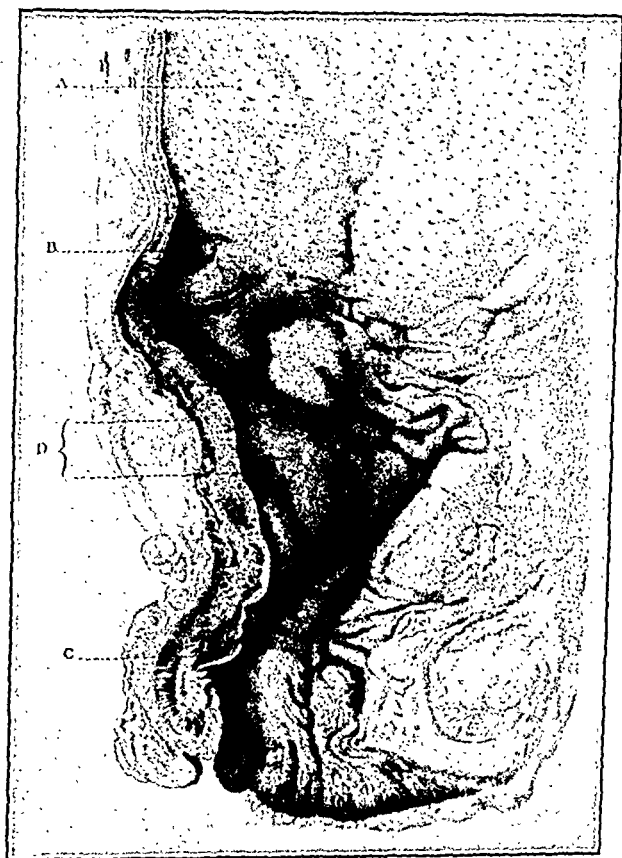


Fig. 1.—This specimen shows about nine inches of the rectum with the anus, preserved in spirits. *A*, normal surface of bowel; *B* to *C*, extent of cavernous nevoid change; *D*, one-half of two ulcers from which fatal bleeding took place. From *B* to *C* the typical cavernous tissue is seen in section. (From Barker, A. E. J.: *Cavernous Naevus to the Rectum Proving Fatal in an Adult from Hemorrhage*, Med. Chir. Tr., London 66: 229-234, 1883.)

found. Transverse colostomy was performed in January, 1921. The postoperative course was characterized by steady improvement in every respect. The menses were established. At the time of publication of the report the patient was leading a fairly normal life.

The second case of Bensaude and Antoine was that of a man, forty-eight years of age, who entered the hospital May 16, 1921, because of

severe rectal hemorrhages. He had suffered previous attacks of "intestinal" hemorrhages in 1888, 1898, 1904, 1908, and 1915. At the time of the third attack in 1904, the patient was treated for an ulcer of the stomach. In 1908, in the course of the fourth attack, the lower intestine "was suspected"; the suspicion was confirmed by Lockhart-Mummery. Bensaude saw the patient in his last illness and made a diagnosis of diffuse hemangioma of the rectum. The patient died on May 27, 1921, eleven days after admission to the hospital. A report of necropsy was not given.

Bancroft, in 1931, reported a case of hemangioma of the sigmoid with satisfactory relief by colostomy and injection of the superior hemorrhoidal vein (after ligation) with 10 c.c. of 40 per cent sodium salicylate. A second operation, performed eleven months later, comprised: (1) exploratory laparotomy, (2) closure of the colonic stoma, (3) cecostomy, and (4) appendectomy. The author stated that the condition might have been a true hemangiomatous tumor, or possibly a dilatation of existing vessels. He presented, in addition to his report, an excellent summary of fourteen reported cases and discussed diagnosis and treatment.

R. Bensaude and A. Bensaude, in 1932, reported two cases of rectal hemangioma in which there was also involvement of the perineum, scrotum, and penis. They mentioned a similar case described by Esau, and one described by Kausch; the latter case was that of a female patient with involvement of the labia majora. They designated, therefore, two types of hemangioma of the rectum: (1) the Barker-Kausch type, which is anorectal, or anorectosigmoidal without cutaneous involvement; (2) the Esau-Bensaude type, which is mucocutaneous or genitoperineorectal. Of fifteen cases, eleven were of Type 1 and four were of Type 2.

#### REPORT OF CASE

A man, aged twenty-eight years, first registered at the Mayo Clinic, Sept. 9, 1925, at the age of sixteen years. His chief complaints were of rectal bleeding and attacks of diarrhea. The trouble began, according to the mother's statement, in the patient's tenth year. The patient was usually constipated, but there were occasional short periods of so-called diarrhea which followed administration of a cathartic. Varying amounts of bright blood were passed at irregular intervals. The patient complained occasionally of pain low in the rectum at the time of defecation.

A year and a half prior to admission to the clinic the patient had an attack of painless hematuria lasting two weeks. He was confined to bed for six weeks with fever and malaise. The significance of this episode will be noted in the report of necropsy.

General physical examination gave essentially negative results. On proctoscopic examination (24 cm.), submucous nodules or lumps seemed to be distributed diffusely and to involve all coats of the bowel. Associated perirectal thickening imparted a sense of fibrosis and limited the mobility of the bowel. The sigmoid was not involved. The disease was believed not to be primary in the rectal mucosa. Biopsy was advised. Diagnosis was withheld.

physically and suffering from anemia and amenorrhea. There were frequent rectal hemorrhages. The abdomen was enlarged and tense; there were visible intestinal contractions. Proctoscopic examination for a distance of 30 cm. revealed a marked enlargement of the "anal veins" (external hemorrhoidal veins?). The rectal lumen was obliterated. The mucosa was pale and edematous, but underlying bluish varicosities were seen. When the mucous membrane was swabbed, the cotton applicators became stained with blood, but no bleeding points or ulceration could be

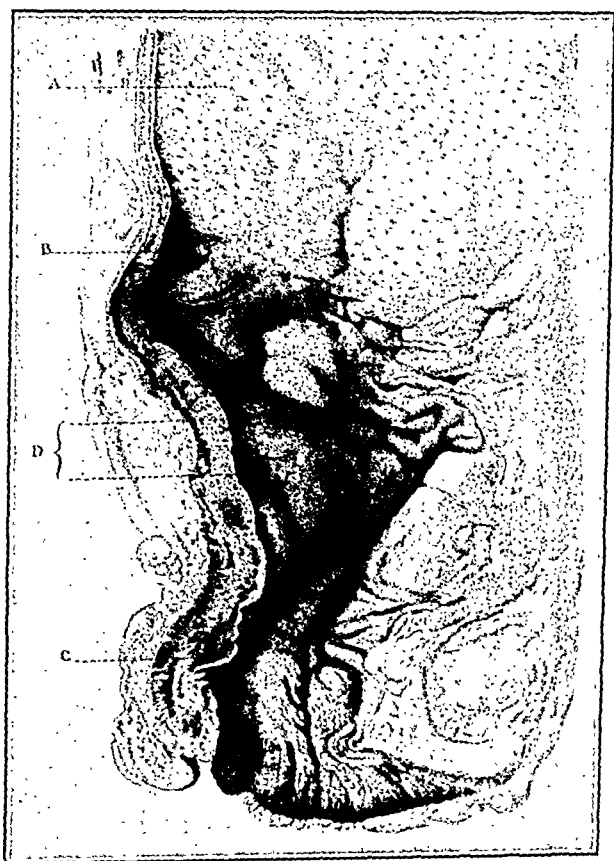


Fig. 1.—This specimen shows about nine inches of the rectum with the anus, preserved in spirits. A, normal surface of bowel; B to C, extent of cavernous nevus; change; D, one-half of two ulcers from which fatal bleeding took place. From B to C the typical cavernous tissue is seen in section. (From Barker, A. E. J.: Cavernous Naevus to the Rectum Proving Fatal in an Adult from Hemorrhage, *Med. Chir. Tr.*, London 66: 229-234, 1883.)

found. Transverse colostomy was performed in January, 1921. The postoperative course was characterized by steady improvement in every respect. The menses were established. At the time of publication of the report the patient was leading a fairly normal life.

The second case of Bensaude and Antoine was that of a man, forty-eight years of age, who entered the hospital May 16, 1921, because of

projecting 1 cm. or more above the surface of the wall of the bowel. The masses all felt cystic but could not be entirely obliterated by pressure. The mucosa was adherent to the masses everywhere and there was no place where this membrane appeared to be normal. There was no ulcerous development, except in two places where needle punctures recently had been made. The color, which appeared to come through the mucosa, was bluish gray and gave the impression that the tumors were either hemangiomatous or melanotic. On account of the long duration of the condition, it was unlikely that the tumors were melanotic. The mucosa overlying one of the lowest masses was split. There was profuse bleeding, which, however, was controlled by pressure and by suture. The inner structure of the mass appeared very much like that of the corpus spongiosum. A specimen was taken for microscopic examination. The examiner stated that the advisability of radium



Fig. 4.—Gross section, stained with hematoxylin-eosin. Mucosal surface is to the right. Anal skin appears at the bottom. The muscular coat is shown passing through the center of the section. In the fatty layer (to the left) are seen several large veins, some of them thrombosed. In the submucosa are shown the large spaces, lined by endothelium and filled with blood.

therapy was to be considered and that if such treatment should prove ineffectual, posterior resection and establishment of a permanent stoma might be the only means of saving life. He said, however, that such an operation would be done at very great risk. In the pathologic report it was stated that the tissue was hemangioma. Three transfusions of blood were given. There was only temporary benefit. On Feb. 14, 1937, the patient suddenly died.

At necropsy there was no evidence of hemorrhage. Nothing was found to account for the sudden death. Hemangiomatous involvement of the pelvis and parenchyma of the right kidney explained the painless hematuria.

Only the pathologic changes which pertain to the subject at hand will be mentioned here. Beginning at the dentate margin, there was a series of nodular,



A specimen was removed for biopsy and the pathologic report was "inflammatory tissue." A course of roentgen therapy was outlined and the first two treatments were given shortly before the patient was dismissed from the clinic.

The patient was registered a second time at the clinic, June 18, 1926. During the period of eight months since his first visit to the clinic he had gained 17 pounds (7.7 kg.) in weight and 2½ inches (6.3 cm.) in height. There was no change in the condition of the rectum and lower sigmoid as observed through the proctoscope.

On Jan. 5, 1937, the patient again visited the clinic. He was pale and weak and suffering from a severe cold. Rectal bleeding had persisted, at intervals, since the time of the previous visit. Hospitalization and supportive treatment were advised.

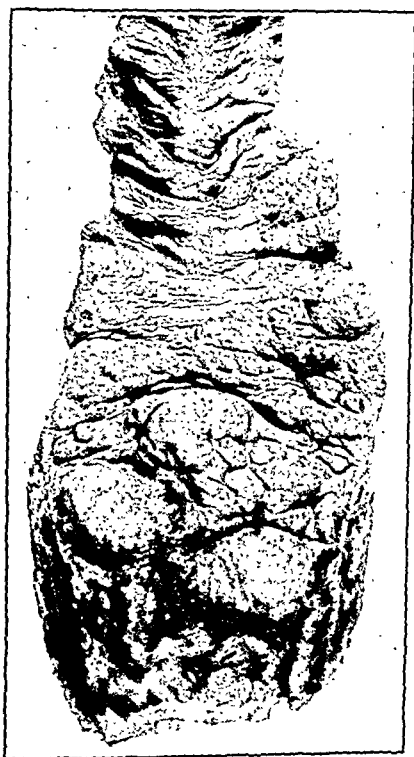


Fig. 2.



Fig. 3.

Fig. 2.—Anus, rectum, and lower sigmoid laid open. The rectal mucosa is elevated and thrown into large folds by the underlying hemangiomatous masses. The transition to normal bowel is abrupt.

Fig. 3.—The specimen represented in Fig. 2 has been sectioned longitudinally. The mucosal surface is to the right. On the left is shown the perirectal fat. Beneath the fatty layer, and just external to the muscular layers, are shown several large, thrombosed veins. The submucosal layer is markedly exaggerated, as shown by the metric scale, because of its involvement by hemangiomatous tissue. The resemblance to erectile tissue is striking.

When the patient's general condition was sufficiently improved, examination was made under anesthesia and the examiner considered that there was a collection of cystic masses which involved the submucosal tissues of the wall of the bowel. The muscular structures possibly were involved also. The masses varied from growths 6 or 8 mm. in diameter to tumors 2 to 4 cm. long and 1 to 2 cm. wide,

The diagnosis of this condition should be determined by proctosigmoidoscopy and biopsy. Digital examination reveals the nodular characteristic of the involved wall. When the proctosigmoidoscope is first introduced, the lumen of the rectum seems to be almost entirely obliterated, yet the instrument usually can be passed without difficulty and an adherent but intact mucous membrane can be seen. The tumors appear bluish through the mucosa, giving a clue as to their blood vascular structure. Further evidence of the vascular character of these masses can be obtained by aspiration of blood from them. Roentgenologic examination may reveal a filling defect in the rectum. However, roentgenologic study of the rectum is not conclusive and the expert proctoscopist usually can make a more adequate study of this organ. That part of the large bowel beyond the reach of the proctosigmoidoscope can be studied by the roentgenologist, but if a lesion is suspected in the rectum or sigmoid, especially when there have been episodes of obstruction of the bowel, it is much safer to make endoscopic examination before barium has been injected for roentgenologic study.

Treatment by radiation has no value. Surgical treatment, that is, establishment of a permanent colonic stoma, followed if possible by radical excision of the affected part of the bowel, is the only means of relief available at present. Antianemic therapy, transfusions, and other supportive measures are essential in preoperative preparation. In the first case reported by Bensaude and Antoine (1923), colostomy alone sufficed to accomplish marked improvement. The great risk of surgical operation in such cases has been mentioned.

The ultimate prognosis, as well as the immediate surgical risk, is grave. Hemangiomatous involvement of other structures, as illustrated by our own case, may be partially responsible for the poor prognosis. It is probable that had our patient survived radical treatment, ultimately he would have been faced by the necessity of removal of the right kidney because of the hemangioma affecting its pelvis and parenchyma.

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submucous projections extending upward for 30 cm. These projections extended into the lumen for 3 cm. The nodules were irregular in size and constituted about five large masses, measuring from 3 to 5 cm. in diameter, which were gathered under the mucosa like grapes. The remainder of the mucous membrane was raised about 1 cm. from the muscularis. The mucosa at the dentate margin was ulcerated; the largest ulcerated area was about 3.5 cm. in diameter. The remainder of the mucosa was greenish black, a color similar to that of the content of the bowel. In the submucosa and the perirectal fat were many dilated networks of veins, some of which were thrombosed (Figs. 2 and 3). Microscopic examination disclosed large sinuses lined by endothelial cells and filled with blood (Fig. 4).

The anatomic diagnosis was hemangioma of the rectum and of the pelvis of the right kidney.

#### COMMENT

The tumor in this case, therefore, was a diffuse, blood vascular mass, composed of blood-filled spaces and resembling erectile tissue, which had invaded all the tunics of the rectum except the mucosa—hence the name “diffuse cavernous hemangioma.”

Bensaude and Antoine have classified hemangiomas as simple and cavernous. The latter type may be either circumscribed or diffuse. Circumscribed cavernous hemangiomas have little tendency toward invasion. They are not rare in the gastrointestinal tract but involve the inside of the cheeks, the lips, the soft palate, the tongue, the stomach, the duodenum, the small and large intestine, and the rectum. Diffuse cavernous hemangiomas have a tendency toward invasion and a predilection for the rectum and sigmoid. The gravity of this condition is owing to severe and frequent hemorrhages.

Several hypotheses relative to the etiology of this condition have been set forth. The most logical conception, however, and one to which the majority of authors on the subject subscribe, is that the entity is congenital in origin.

The pathologic anatomy in our case coincides closely with the descriptions given by Barker and by Kausch. The tumor is composed of blood vascular tissue characterized grossly by rather large spaces filled with blood. The resemblance to erectile tissue is striking. The sinuses are lined by endothelium. The tendency toward invasion of the wall of the bowel is well shown in our specimen. The overlying mucosa is adherent to the tumor but is intact.

The clinical course is characterized particularly by bleeding from the rectum. In several of the previously reported cases, and in our own, the bleeding appeared in early childhood. The losses of blood vary both in frequency and in amount. The result is severe hypochromic anemia. There may be considerable so-called rectal pain. Our patient complained bitterly of tenesmus and pain in the rectum during the final stages of his illness. In several reported cases the patient has died exsanguinated. The sudden death of our patient has not been explained.

lesions were almost always in this space; whereas, subphrenic abscesses complicating perforated peptic ulcer were in either the superior or inferior regions.

The etiology in practically all cases was some abdominal infection. The trio, perforated peptic ulcer, appendicitis, and cholecystitis, accounted for over 70 per cent of the abscesses. Perforated ulcers came first in the list, being responsible for 18 of the 50 cases (36 per cent). Six of these developed in individuals who either refused primary surgery or, because of atypical findings, were operated upon for their perforation only after a delay of several days, or not at all.

A fact that seems worth recording is that in all instances of operation for a perforation rubber tissue drains were placed in the upper abdomen. In all but 2, the perforations were merely closed without further surgery. In 1, a Billroth II resection was performed, and in another, a Judd type of pyloroplasty was done.

Thirteen of the 50 cases (26 per cent) followed acute appendicitis or appendectomy and constituted the second largest group. Two of the appendices were not acutely inflamed (one being removed following a subtotal hysterectomy), indicating that the technique of appendectomy might be improved. In the great majority of cases there was perforation of the appendix with a complicating generalized peritonitis. In one instance a subphrenic abscess was not suspected until a year after the removal of a perforated appendix, when the sudden evacuation of foul pus through a bronchus led to further examination.

Although gallbladder disease is not commonly considered as a cause of subphrenic abscess, surgery on the gallbladder or perforation of an acutely inflamed gallbladder gave rise to 6 such infections (12 per cent). Two of these followed cholecystectomy and both had biliary duct drainage. Five of the 6 died. All of these abscesses were accessible to drainage through an anterior approach.

The fourth group (4 cases, 8 per cent) developed from perforations of amebic liver abscesses. All of these gave preceding history of vague abdominal or gastrointestinal distress of many years' duration. In them the subphrenic abscess responded to treatment and all recovered.

Finally, there were 8 cases associated with miscellaneous lesions; 2 resulted from a perforation of a diverticulum of the large bowel; 2, from injury to the liver (automobile accidents); 2, from infected abortions; 1, from a pleural empyema with multiple rib resections; and 1, from a urethral stricture with perinephritic abscess.

The recognition of a subphrenic abscess, as indicated by a study of the cases in this series, is quite difficult, and this difficulty of recognition is apparently one of the chief factors responsible for the high mortality. Approximately one-third of the fatal cases were not operated upon, chiefly because the subphrenic abscess was not recognized.

## SUBPHRENIC ABSCESS

### FACTORS IN THE HIGH MORTALITY

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**A**BSCCESS of the subphrenic region is a rather uncommon lesion. At the Los Angeles General Hospital, during a ten-year period from 1926 to 1936, there were only fifty such infections proved by either surgery or autopsy. During this time the average yearly admissions to the surgical services were over 5,000 patients. Relatively few surgeons encounter a sufficient number of such cases to make practical deductions as to their management. To the man in general practice doing occasional surgery, this complication often brings a feeling of helplessness and dread.

That this feeling is justified may be gathered from reports of mortality in subphrenic abscess, which generally vary from 30 per cent to 80 per cent. The mortality in the fifty cases at the Los Angeles General Hospital, operated and nonoperated, was 50 per cent. With his report of 9.7 per cent mortality, Alton Ochsner has pointed out that more favorable results are possible.

The improvement in the management of these abscesses, as emphasized particularly by Ochsner (an improvement that has led to the lower mortality figures), has not, however, been generally recognized and followed.

For surgical purposes, Ochsner has described the subphrenic space as the area located between the diaphragm above and the transverse mesocolon and transverse colon below. This area is divided by the liver into a suprahepatic and an infrahepatic portion. The suprahepatic space, the more important of the two, is divided into one extraperitoneal space (the bare area) located within the confines of the coronary ligament, and several intraperitoneal spaces. The falciform and round ligaments divide the intraperitoneal spaces into right and left ones. On the left side, the left prolongation of the coronary ligament, the left lateral or triangulate ligament, passes backward to lie at the posterior edge of the liver. This gives rise to only one left superior space. On the right side, the right lateral ligament passes anteriorly, dividing the right superior space into an anterior and posterior.

Of the abscesses in this series, all were on the right side. The majority were in the posterior-superior space. Following appendicitis the

uncertainty on the part of the surgeon concerning the presence of pus. However, from a study of the case histories, the diagnosis would seem to be quite evident, but in many instances delay was permitted. Usually there is a history of a recent attack of acute appendicitis or perforation of a peptic ulcer. The temperature curve is of the septic type and is associated with leucocytosis. X-ray shows a high diaphragm on one side; a lateral view may show this elevation to be anterior or posterior; and on fluoroscopy the diaphragm is often fixed at the place of elevation. These examinations are frequently repeated in the hope that improvement will follow; drainage is delayed or not done. This delay is the second factor in the high mortality.

Four of our cases of abscesses associated with gallbladder lesions occurred following perforation in acute cholecystitis treated by the method of watchful expectancy.

In the method of draining the abscess is to be found the third, and probably the most important, factor, in the high mortality of the present group of cases. Drainage was accomplished in a variety of ways: aspiration through a needle, by means of a trochar and catheter, by rib resection, and through the pleural space (in one and two stages), through the abdomen; and in very few cases by the extrapleural and extraperitoneal route advocated by Ochsner.

In 1 of the 2 cases of lacerated liver, repeated aspiration through the ninth and tenth intercostal spaces transversing the right pleural cavity effectually emptied a subphrenic collection of cloudy bile-stained fluid which was sterile on culture.

Trochar drainage was used in 6 cases. One was amebic in origin, and it is to be noted that this type of lesion cleared up under various methods of treatment and did not give rise to a pleural empyema when the pleura was contaminated. Apparently this type of abscess is generally free of bacteria. This is in accord with the excellent results at present obtained by the combined use of emetine and multiple aspirations in amebic liver abscess. Another case, effectively treated by trochar and catheter drainage, was one in which an abscess was found a year after a perforated appendix had been removed. The success of this type of treatment was possible in this instance probably because of two factors. The pus had become sterile and the costophrenic angle of the pleura had probably become obliterated. No empyema followed. A third case developed a pleural empyema after the use of a trochar; and a fourth died four days after its insertion.

Aspiration through the pleural space as a diagnostic procedure quite obviously gave rise, in a number of instances, to pleural infection. Instillation of iodine or mercurochrome in the needle tract did not seem to prevent such infection.

Some of these cases, however, were complicated and the patients probably would not have recovered even after the benefit of drainage. Since over 60 per cent of the abscesses resulted either from perforation of a peptic ulcer or inflammation of an appendix, merely thinking about the subphrenic infection as a possible postoperative complication would help considerably in its recognition in connection with these catastrophies. The experience of this series indicated that when a subphrenic abscess was suspected it was usually present.

The following cases of subphrenic abscess are of interest, from the standpoint of difficulty of recognition and delay in treatment.

#### CASE REPORTS

CASE 1.—Male, aged twenty-three years, was operated upon July 22, 1932. A right rectus incision was made and a gangrenous perforated appendix with generalized peritonitis found. Appendectomy with drainage was performed. The patient continued to run a septic temperature postoperatively, otherwise he seemed all right. On Aug. 28, 1932, he developed a severe cough with blood-tinged sputum, dyspnea, and cyanosis, and he was believed to have pulmonary embolism. The patient died Aug. 31, 1932.

*Autopsy:* Large subphrenic abscess, right posterior walled-off pleural empyema in region of right base, and hepatization of right base. Both abscesses contained gram-negative rods and gram-positive cocci.

CASE 2.—Male, aged thirty-eight years, entered the hospital Oct. 23, 1932, with history and findings typical of perforated peptic ulcer. X-ray examination showed air under the right diaphragm. Laparotomy revealed a great deal of cloudy fluid and small perforation at the pylorus. The perforation was closed with gastrointestinal purse-string sutures; all free fluid was aspirated and a Penrose drain was placed in the subphrenic space. The patient improved, but ten days later he began to run septic temperature. X-ray indicated high right diaphragm, and the white blood count was 16,000. The patient complained of chilly sensations and pain over lower right thorax. A tender mass became palpable below right costal arch. On Nov. 20, 1932, an incision paralleling the costal arch was made and the abscess cavity drained. The patient died a few hours after surgery. Autopsy was not obtained.

In Case 2 it is worth noting that a drain was placed in the upper abdomen and that the abscess was not evacuated until almost a month after the onset of the septic temperature.

Particularly striking about the manner of death of some of these cases, especially those in whom the presence of subphrenic pus was not recognized, is the fact that it was generally sudden and dramatic, suggesting some new accident. The patient appeared fairly well at one moment, but in a short time became dyspneic, cyanotic, and cold. The pulse was rapid and thready. In such cases the diagnosis often made before death was pulmonary embolism.

Delay in instituting surgical drainage of the abscess is quite commonly noted in a study of these histories and is apparently due to the

## URETHRAL URINARY EXTRAVASATION

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IT IS GENERALLY conceded that the mortality from the extravasation of urine is quite high. Statistics of larger groups of cases give the average mortality at 40 to 43 per cent.<sup>1-3</sup> In our series of 15 consecutive cases occurring in the past ten years, there was only 1 death (6.6 per cent).

### ETIOLOGY

It is interesting to note that urinary extravasation rarely results from complete rupture of the urethra. One prerequisite for urinary extravasation, therefore, may be a urethra which is uninterrupted except for one small break. In 5 cases of complete rupture of the urethra seen by the authors, there was no instance of extravasation, presumably because of loss of the desire to urinate or of the expulsive force; consequently urine is not forced into the tissues.

In most instances extravasation occurs only in the presence of a stricture of the urethra, although a few cases have been reported in which there was no stricture. These strictures are, in the main, of gonorrheal origin, but they may be traumatic. Traumatic stricture was present in 5 of our 15 cases. This means that urinary extravasation is a more frequent complication of traumatic than of gonorrheal strictures.

TABLE I  
ETIOLOGY OF EXTRAVASATION

Gonorrheal stricture	8
Traumatic stricture	5
Trauma following sounds	2
8 colored    7 white	
Average age	45 years

The beginning of urinary extravasation probably occurs in an infected gland or pocket of scar tissue in the urethra resulting from some old infection or injury located proximal to a stricture. This pocket increases in size as a result of repeated straining in order to void until its wall becomes paper thin. When rupture of this wall finally occurs, urine escapes into the surrounding tissue with each micturition. The amount of urine escaping probably varies with the size, location, and shape of the opening and with the severity of the stricture. In some cases the urine escapes very slowly and leads to a condition resembling

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Ten cases were drained through the abdomen. Five (50 per cent) died. In 4 of these, pus was spilled into the general peritoneal cavity at the time of the operation. All but 1 were drained through a rectus incision.

The great majority were drained through the pleural space following rib resection. This included 19 cases, of which 7 (36 per cent) died; 7 others (36 per cent) developed a pleural empyema as a complication of the treatment. Of those terminating fatally, 6 probably had pleural infection. Thus, in relatively few cases was it possible to enter the pleural space without causing contamination of sufficient extent to involve the necessity of subsequent drainage, or even the possibility of early death. Suturing the pleural surfaces and using a two-stage transpleural approach did not prevent pleural contamination.

The method of drainage employed by Ochsner was used in only 3 cases of this series. In this approach the patient lies on the sound side; the twelfth rib is resected subperiosteally and the abscess cavity over the liver entered by gentle dissection—the diaphragmatic peritoneum being stripped away from the diaphragm. Neither the general peritoneal cavity nor the pleural cavity is entered. Local anesthesia may be used. An additional advantage of rib resection at this site is the possibility of employing an aspirating needle under direct vision to locate and drain a subhepatic abscess.

For an abscess located anteriorly an incision may be made immediately below and parallel to the costal arch down to the peritoneum. Then, gently stripping the peritoneum away from the under surface of the diaphragm, entry is gained to the pocket of pus without contamination of the general peritoneal cavity. There is much less shock to such a procedure in which neither the pleural nor peritoneal cavity is entered.

In conclusion, the three factors to be emphasized in reducing the high mortality of subphrenic abscess are:

1. Earlier diagnosis—keeping in mind the occurrence of subphrenic infection after perforated ulcers and appendices.
2. Earlier drainage—when the diagnosis is made, drain without delay.
3. A more frequent use of the extrapleural and extraperitoneal approach for purposes of drainage.

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perineal fascia), the reflected portion of which forms the superficial layer of the urogenital diaphragm. In front of this layer of Colles' fascia is the superficial perineal pouch which is enclosed by the union of the deep and superficial layers of Colles' fascia in front of the anus. Both layers of Colles' fascia are firmly attached to the ischiopubic rami and ischial tuberosity, but, its superficial layer covers the scrotum and penis, and extends up over the abdomen to become continuous with the deep layer of the superficial fascia of the abdomen (Scarpa's fascia). In the perineal type of urinary extravasation the original swelling in the perineum soon extends to the scrotum and penis, and later over the

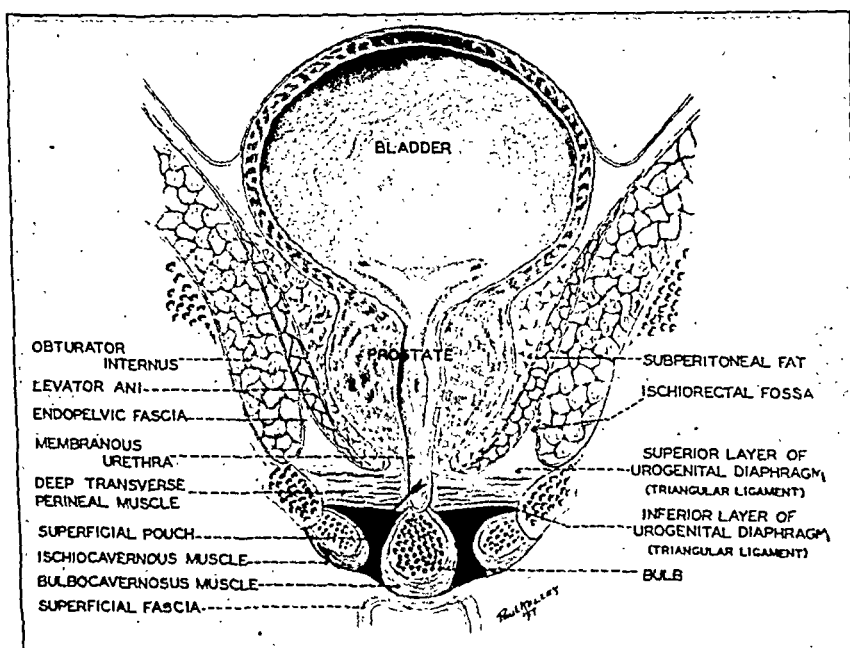


Fig. 2.—Frontal view showing direction of urinary extravasation in the perineal type.

abdomen, in some cases as high as the axillae. Extension into the thigh is prevented by the attachment of Scarpa's fascia to the inguinal ligament. Figs. 1 a and 2 illustrate the direction of the perineal type urinary extravasation.

In the pelvic type of extravasation the point of rupture of the urethra is posterior to the urogenital diaphragm (triangular ligament). The deep layer of the urogenital diaphragm is formed by the inferior layer of the endopelvic fascia and forms the floor of the ischioanal fossa. Anteriorly there is a definite recess extending well toward the body of the pubes and posteriorly there is a recess below the lower edge of the gluteus maximus. Rupture may occur also into the subperitoneal space from which urine may later break into the peritoneal cavity.

elephantiasis of the scrotum, as described by Harry Rolnick.<sup>4</sup> Sometimes extravasation has resulted from the dilatation of a urethral stricture either at once or after an interval. Two such cases are included in this series. The etiology of extravasation as seen by us is summarized below in Table I.

Other causes of urinary extravasation from the urethra are the obstruction from a urethral stone, the rupture of a periurethral abscess; in a few cases, occurring in infancy, the etiology is not clear.

#### DIRECTION OF EXTRAVASATION

Since 66 per cent of urethral strictures involve that portion of the urethra beginning three-fourths inch behind, and ending one inch in front of the triangular ligament,<sup>5</sup> it is natural that most cases of urinary extravasation should have their origin here. In fact, urinary extravasation rarely occurs in any other location. The direction which extrava-

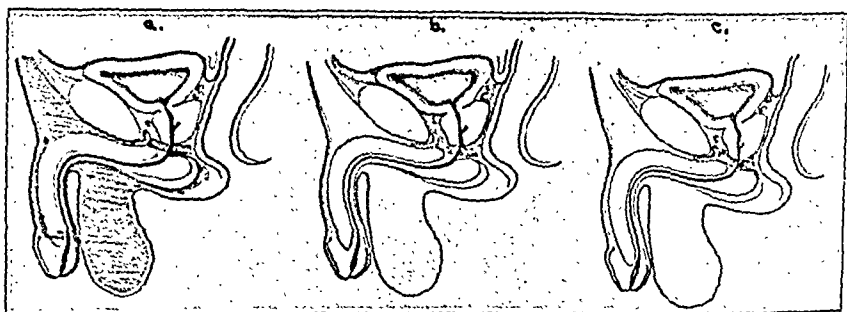


Fig. 1.—Lateral view showing direction of urinary extravasation in the perineal, pelvic, and intraligamentous types (from Meredith Campbell). (a) When lesion is anterior to the triangular ligament, a course bounded by Colles' and Scarpa's fasciae is pursued. (b) When extravasation occurs on the pelvic side of the triangular ligament, retroprosthetic, perirectal, and ischioirectal infiltrations are most commonly observed, although perivesical and prevesical involvement may occur. (c) If the extravasation originates within the triangular ligament, extension occurs in either direction, most often externally.

sated urine will take is dependent upon the relationship of the point of rupture to the fascial planes of the surrounding fascia.

Urinary extravasation from the urethra is usually classified according to its origin as: (1) penile, within Buck's fascia; (2) perineal, anterior to the triangular ligament; (3) pelvic, posterior to the triangular ligament (either into the ischioirectal fossa or subperitoneal space); and (4) intraligamentous, within the triangular ligament.

Extravasation within the confines of Buck's fascia is uncommon and is due to a rupture in the penile urethra. In these cases the swelling is limited to the penis alone. The extent of Buck's fascia and the appearance of such extravasation are illustrated by Miley Wesson.<sup>6</sup>

In the perineal type of urinary extravasation the point of rupture is anterior to the urogenital diaphragm (triangular ligament). This means that the extravasated urine will be limited by Colles' fascia (superficial

perineal fascia), the reflected portion of which forms the superficial layer of the urogenital diaphragm. In front of this layer of Colles' fascia is the superficial perineal pouch which is enclosed by the union of the deep and superficial layers of Colles' fascia in front of the anus. Both layers of Colles' fascia are firmly attached to the ischiopubic rami and ischial tuberosity, but, its superficial layer covers the scrotum and penis, and extends up over the abdomen to become continuous with the deep layer of the superficial fascia of the abdomen (Scarpa's fascia). In the perineal type of urinary extravasation the original swelling in the perineum soon extends to the scrotum and penis, and later over the

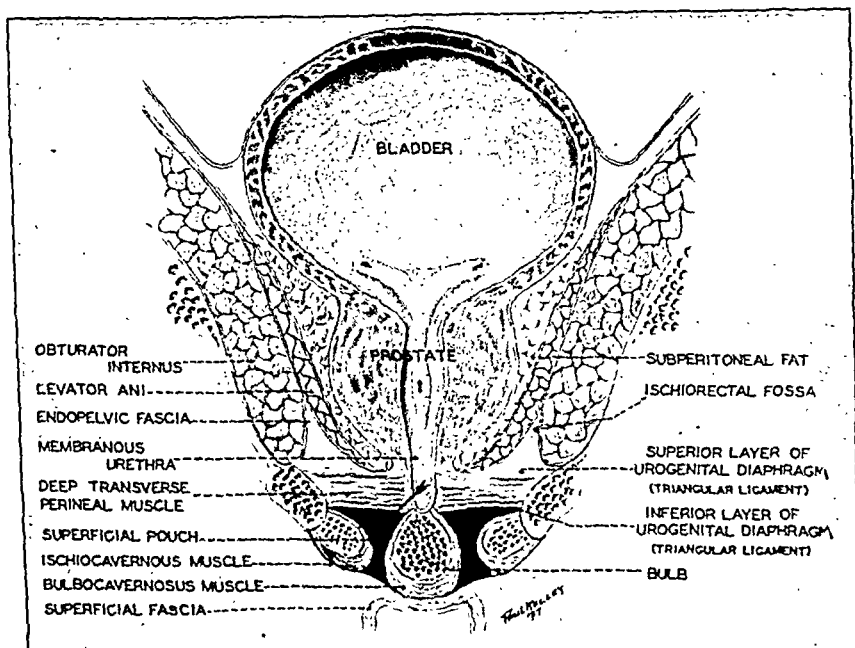


Fig. 2.—Frontal view showing direction of urinary extravasation in the perineal type.

abdomen, in some cases as high as the axillae. Extension into the thigh is prevented by the attachment of Scarpa's fascia to the inguinal ligament. Figs. 1 a and 2 illustrate the direction of the perineal type urinary extravasation.

In the pelvic type of extravasation the point of rupture of the urethra is posterior to the urogenital diaphragm (triangular ligament). The deep layer of the urogenital diaphragm is formed by the inferior layer of the endopelvic fascia and forms the floor of the ischioanal fossa. Anteriorly there is a definite recess extending well toward the body of the pubes and posteriorly there is a recess below the lower edge of the gluteus maximus. Rupture may occur also into the subperitoneal space from which urine may later break into the peritoneal cavity.

In the pelvic type of urinary extravasation there is at first a swelling in the perineum and, as a general rule, extension into the suprapubic recess. Figs. 1 b and 3 illustrate the direction of urinary extravasation in the pelvic type.

The intraligamentous type, which follows rupture of the urethra between the layers of the urogenital diaphragm (Fig. 1 c), is generally considered to have a better prognosis than the other three since the extravasation is often confined within the layers of the diaphragm.<sup>7</sup> However, it may rupture, either externally or internally, producing either the pelvic or perineal type, or subcutaneously with extravasation into the gluteal region.

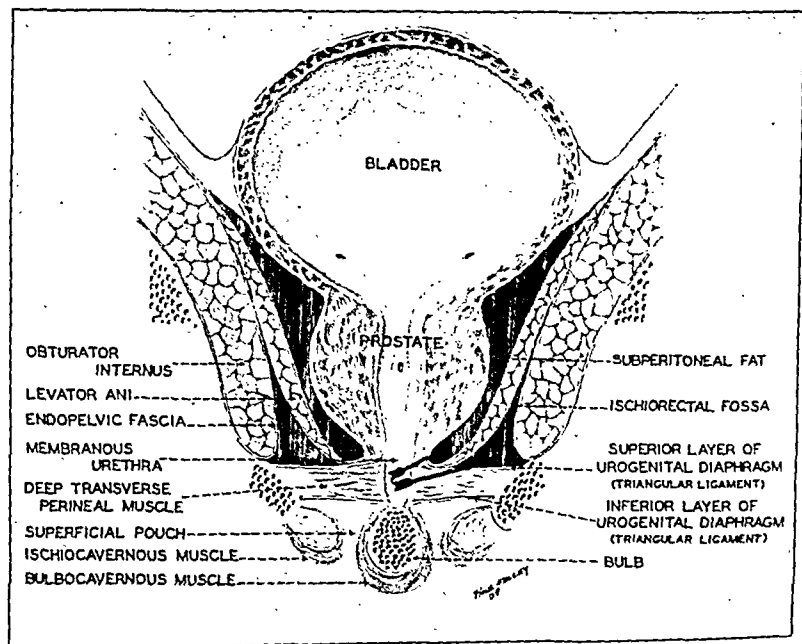


Fig. 3.—Frontal view showing direction of urinary extravasation in the pelvic type.

In our series 11 were perineal, 3 were pelvic, and 1 was pelvic and later perineal. The last may have been an instance of rupture between the layers of the urogenital diaphragm. There was no case of extravasation within Buck's fascia, although most of the perineal type had considerable swelling of the penis.

#### SYMPTOMS AND SIGNS

The patient complains of a sudden sharp, spontaneous pain, usually in the perineum, followed by the development of swelling and increasing difficulty in urinating. The location of the swelling depends upon the location and size of the rupture and, to some extent, upon its duration.

In most instances there has been previous difficulty in micturition, due either to a gonorrheal or to a traumatic stricture. When first seen, the patient generally feels quite ill, and there may be complete urinary retention.

On examination, the affected parts are at first greatly enlarged and quite tender to the touch. The patient appears toxicemic and may have chills and fever. The pulse is somewhat faster than normal. The white blood count is elevated ranging from 14,000 to 28,000 in the acute stages. The urine when first obtained contains considerable albumin. The N.P.N. and creatinin may be elevated. Later he may exhibit mental confusion progressing to delirium and coma.

As the extravasation progresses necrosis of tissue occurs, particularly in the perineal type. There may be, therefore, darkened areas on the scrotum and the penis if the extravasation has been of sufficient duration. It is probable that necrosis is not due to the irritative properties of urine but rather to the pressure of the urine which cuts off the blood supply of the tissues.

#### TREATMENT

These patients are usually desperately ill and require prompt treatment. Their general condition has often been impaired by the antecedent urinary difficulty with its attendant loss of rest and backflow of urinary products. In addition, the patient with urinary extravasation has increased difficulty in urination from the extravasation itself, as well as imminent or established uremia, and also a severe toxemia from the absorption of the products of degenerating tissue.

Free drainage of the bladder should be provided and adequate incisions for release of extravasated urine and of necrotic tissue should be made. It is better not to waste time in attempting to dilate the already injured urethra. To do so may add just the amount of trauma necessary to make the ending fatal. The perineal cystotomy advocated by some does not seem logical, since the insertion of a catheter into the

TABLE II  
TREATMENT OF EXTRAVASATION

Suprapubic cystotomy		8
Cystotomy only	0	
Cystotomy and scrotal incision	5	
Cystotomy and suprapubic incision	3	
Catheter drainage		7
Internal urethrotomy and incision	1	
Sounds and scrotal incision	4	
Sounds and spontaneous rupture	2	
	15	
Deaths	1	
Recovered	14	

bladder must further damage already injured and infected tissue. Good judgment as to the type of procedure to be employed is a prime requisite for the proper treatment of urinary extravasation. The therapy employed in our 15 cases is summarized in Table II.

*Discussion.*—It may be that the better results which we present are due to the fact that the patients were seen earlier than are those in the hospitals of larger cities where derelicts abound. Certainly few are ever seen in private practice. In this group only 2 were private patients.

#### SUMMARY

Urinary extravasation from the urethra is accompanied by profound toxemic symptoms from the absorption of the products of damaged tissue and is often accompanied by increasing uremia because of urinary obstruction. The condition is readily recognizable and can be divided into penile, perineal, pelvic, and intraligamentous types. Of these the perineal is by far the most common. The mortality is usually high. Prompt treatment by means of diversion of the urine and by adequate incisions for the extrusion of dead and dying tissue is necessary. Fifteen cases are reported with one death.

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# CONCERNING RENAL FUNCTION AND STRUCTURE FOLLOWING TRAUMA OF THE KIDNEY

## AN EXPERIMENTAL STUDY\*

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THE modern principles of renal surgery demand the preservation of function and the restoration of structure in a diseased organ. The experimental studies of renal function herein recorded, correlated with the pathologic changes secondary to direct injury, are offered as a rational basis for the same intelligent conservatism in the treatment of traumatic lesions of the kidney.

### STUDIES OF RENAL FUNCTION†

These experiments were divided into two series: the first was designed to determine the effect of renal trauma on the function of the single kidney of rabbits previously subjected to unilateral nephrectomy; the second, to determine the effect of severe unilateral trauma on the renal function of normal animals and the ability of the injured kidney to recover by subsequent removal of the untraumatized organ.

#### FIRST SERIES

*Method.*—Male rabbits weighing between 3¾ and 4¾ pounds were used. No food or water was given after five o'clock in the afternoon of the day preceding the experiment.

The normal renal function of the intact animal was first determined as follows:

The rabbit was placed in a supine position on the animal board. Blood for determination of the nonprotein nitrogen was collected by cardiac puncture. The prepuce was then retracted and a sterile soft rubber catheter, size No. 10 F., was passed into the bladder. The urine was aspirated with a syringe and put aside for later routine analysis. The bladder was irrigated with tap water until the return was clear; the catheter was clamped and left in place.

One hundred to one hundred and fifty cubic centimeters of normal saline solution (depending on the size of the rabbit) were given by gastric tube in order to stimulate a satisfactory flow of urine. One cubic centimeter of phenolsulphonephthalein, containing 6 mg. of the dye, was then injected into a marginal vein of the ear and the exact time recorded at the completion of the injection. The bladder was aspirated through the catheter every ten minutes during the first hour and at half-hourly intervals during the second hour. At each aspiration, the bladder was irrigated with a fixed amount of tap water in order to wash out all the dye therein contained.

\*Read at the Annual Meeting of the Halsted Club, Philadelphia, Pa., Dec. 5, 1936. Received for publication, Sept. 28, 1937.

†Two clinical cases and part of these experimental data have been reported in a previous paper.<sup>1</sup>



Each specimen was alkalized with sodium hydroxide, diluted, and the amount of dye computed by comparison with a series of commercially prepared standard solutions.

Right nephrectomy was performed with sterile surgical technique under basal anesthesia of urethane, supplemented by ether. At intervals, varying from one week to one month after the immediate convalescence, all the preoperative studies were repeated and closely checked.

The left kidney was then traumatized. The organ was exposed retroperitoneally, delivered from the renal fossa, and allowed to lie on the gauze covering the lumbar muscles and skin at the posterior angle of the incision. The anterior surface of the kidney was struck smartly several times with the rounded end of a Wedgewood pestle, about one inch in diameter.

Determination	Color	Reac- tion	Urinalysis				P.S.P. Test											Total	N.P.N.
			Sp. gr.	Alb.	Sug.	Sediment	Minutes												
							10	20	30	40	50	60	90	120					
Normal Control	V. Cldy. Yel.	Alk.	1.042	Neg.	Neg.	Phosphates.....	38	31	10	7	4	2.5	4	2.5	99	40			
RIGHT NEPHRECTOMY																			
Normal L. Kid.	Cldy. Yel.	Alk.	1.040	Neg.	Neg.	Neg.....	40	21	11	6	4	3	3	3	91	44			
OPERATIVE CONTUSION OF LEFT KIDNEY																			
1st P. O. Day..	Cldy. Red. Yel.	Neut.	1.013	V.H.T.	Neg.	R.B.C., W.B.C., E.C.	2	3	2.5	4	1.5	1.5	4.5	3.5	22.5	150			
2nd Day.....	Cl. Pink. Yel.	Acid	1.008	H.T.	Neg.	R.B.C., W.B.C., E.C.	7	6	4	3.5	3	2.5	6	6	38	160			
3rd Day.....	Cl. Amber	Acid	1.012	T.	Neg.	R.B.C., W.B.C., E.C.													
4th Day.....	Cldy. Yel.	Acid	1.002	T.	Neg.	H.C.	7	7	4	3.5	3	2.5	8	7	42	129			
						R.B.C., W.B.C., E.C.													
6th Day.....	Cl. Yellow	Neut.	1.007	S.P.T.	Neg.	G.C.	2	3.5	3.5	3	3	3.5	9	5	32.5	79			
8th Day.....	Cldy. Yel.	Alk.	1.027	Neg.	Neg.	R.B.C., W.B.C., E.C.	18	9	9	6.5	4	13	6.5	70		71			
10th Day.....	Cldy. Amb.	Acid	1.032	S.P.T.	Neg.	W.B.C., E.C.	33	15	11	7	5	3	9	4	87	43			
14th Day.....	Cldy. Yel.	Alk.	1.028	Neg.	Neg.	W.B.C., E.C.	33	18	12	7	4	3	7	3.5	87.5	33			
21st Day.....	Cldy. Yel.	Alk.	1.030	Neg.	Neg.	W.B.C.	32	25	12	7	4.5	4	6	3	93.5	39			
28th Day.....	Cldy. Yel.	Alk.	1.030	Neg.	Neg.	Phosphates	40	22	8	7	4	3	6	3	93	36			
28th Day.....	Cldy. Yel.	Alk.	1.032	Neg.	Neg.	W.B.C., E.C.	40	30	11	4	4	3	7	2.5	101.5	54			

Table I.—Detailed studies of the function of a single kidney following trauma of moderate severity. (From Powers: New York State J. Med. 36: 1, 1936.)

The contused and bleeding organ was then replaced and the wound closed in layers with fine silk.

The function of this single traumatized kidney was studied daily for four days, again on the sixth, eighth, tenth, and fourteenth postoperative days, at the end of three weeks, and finally at the expiration of one month.

**Results.**—Six animals were included in this series. Three of them, in which the kidney was subjected to trauma of moderate severity, survived. The detailed studies of one animal are presented in Table I. The determinations before and after removal of the right kidney represent the average of two or more observations; those after contusion of the left kidney are single determinations.

Determination	Color	Reac-	Sp. gr.	Analysis		Sug.	Sediment	P.S.P. Test											Total	N.P.N.
								Minutes												
								10	20	30	40	50	60	90	120					
Normal Control.	Cldy. Yel.	Alk.	1.026	Neg.	Neg.	Phosphates.....	12	45	20	7	3.5	3	3	3	96	5	37			
RIGHT NEPHRECTOMY																				
Normal L. Kid.	Cldy. Yel.	Alk.	1.040	Neg.	Neg.	Phosphates.....	36	22	15	7	5	3	5	3	96		40			
OPERATIVE CONTUSION OF LEFT KIDNEY																				
1st P. O. Day..	Bloody	Neut.	1.016	V.H.T.	Pos.	Loaded R.B.C.....	0.5	0.5	0.2	0	3	0	1	5	0.5	3.5	173			
2nd Day.....	Clear Yel.	Acid	1.010	H.T.	Neg.	R.B.C., W.B.C., E.C.,														
3rd Day.....	Dead					C.....	1.0	0.7	0.7	1.0	0.7	0.5	2	1.7	8	3	240			

Table II.—Detailed studies of the function of a single kidney following severe contusion and extensive trauma. (From Powers: New York State J. Med. 36: 1, 1936.)

The effect of trauma on the function of the single kidney, as measured by the total excretion of phenolsulphonephthalein and the nonprotein nitrogen of the blood, are presented graphically for the group in Figs. 1 and 2. These indices of renal function returned to normal levels within a period of fourteen days after the injury.

The three rabbits whose single kidney was severely traumatized died on the second and third day after contusion. The urine was grossly bloody; the specific gravity was low; heavy traces of albumin were present; the output was diminished; and in one instance complete anuria occurred. Either none or minimal amounts of phenolsulphone-

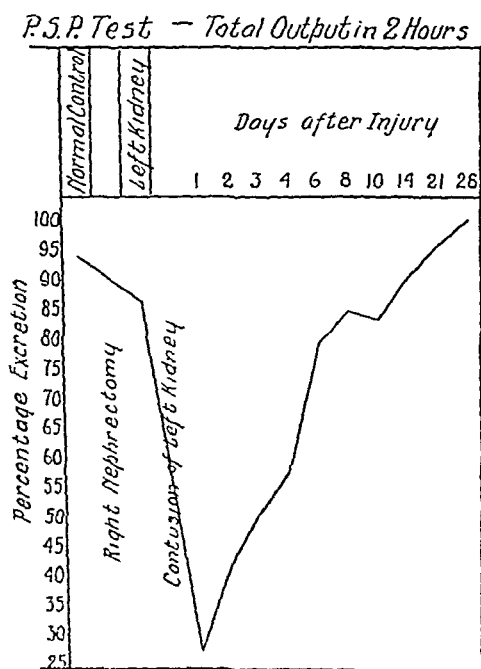


Fig. 1.—Composite curve illustrating the effect of renal trauma of moderate severity on the ability of the single kidney of nephrectomized rabbits to excrete phenolsulphophthalein. (From Powers: New York State J. Med. 36: 1, 1936.)

phthalein were excreted and the nonprotein nitrogen of the blood rose rapidly to high levels. The detailed studies of one such animal are presented in Table II.

**Conclusion.**—Renal trauma of moderate severity impairs the ability of the kidney to excrete urine of normal concentration, reduces the early elimination of phenolsulphonephthalein, decreases the total excretion of the dye, and causes an abrupt and conspicuous rise in the nonprotein nitrogen of the blood. Albumin, red cells, white cells, and casts of various types are found in the urine. The restoration of normal renal function is prompt and complete.

Each specimen was alkalized with sodium hydroxide, diluted, and the amount of dye computed by comparison with a series of commercially prepared standard solutions.

Right nephrectomy was performed with sterile surgical technique under basal anesthesia of urethane, supplemented by ether. At intervals, varying from one week to one month after the immediate convalescence, all the preoperative studies were repeated and closely checked.

The left kidney was then traumatized. The organ was exposed retroperitoneally, delivered from the renal fossa, and allowed to lie on the gauze covering the lumbar muscles and skin at the posterior angle of the incision. The anterior surface of the kidney was struck smartly several times with the rounded end of a Wedgewood pestle, about one inch in diameter.

Determination	Color	Reac-	Sp. gr.	Alb.	Sug.	Sediment	P.S.P. Test												Total	N.P.N.
							Minutes													
							10	20	30	40	50	60	80	120						
Normal Control	V. Cldy. Yel.	Alk.	1.042	Neg.	Neg.	Phosphates.....	38	31	10	7	4	2.5	4	2.5	99	40				
RIGHT NEPHRECTOMY																				
Normal L. Kid.	Cldy. Yel.	Alk.	1.040	Neg.	Neg.	Neg.....	40	21	11	6	4	3	3	3	91	44				
OPERATIVE CONTUSION OF LEFT KIDNEY																				
1st P. O. Day..	Cldy. Red. Yel.	Neut.	1.013	V.H.T.	Neg.	R.B.C., W.B.C., E.C.	2	3	2.5	4	1.5	1.5	4.5	3.5	22.5	150				
2nd Day.....	Cl. Pink. Yel.	Acid	1.008	H.T.	Neg.	R.B.C., W.B.C., E.C.	7	6	4	3.5	3	2.5	6	6	38	160				
3rd Day.....	Cl. Amber	Acid	1.012	T.	Neg.	R.B.C., W.B.C., E.C.														
4th Day.....	Cldy. Yel.	Acid	1.002	T.	Neg.	H.C.	7	7	4	3.5	3	2.5	8	7	42	129				
6th Day.....	Cl. Yellow	Neut.	1.007	S.P.T.	Neg.	R.B.C., W.B.C., E.C.	2	3.5	3.5	3	3	3.5	9	5	32.5	79				
8th Day.....	Cldy. Yel.	Alk.	1.027	Neg.	Neg.	R.B.C., W.B.C., E.C.	18	9	9	6.5	4	4	13	6.5	70	71				
10th Day.....	Cldy. Amb.	Acid	1.032	S.P.T.	Neg.	W.B.C., E.C.	33	15	11	7	5	3	9	4	87	43				
14th Day.....	Cldy. Yel.	Alk.	1.028	Neg.	Neg.	W.B.C., E.C.	33	18	12	7	4	3	7	3.5	87.5	33				
21st Day.....	Cldy. Yel.	Alk.	1.030	Neg.	Neg.	W.B.C.	32	25	12	7	4.5	4	6	3	93.5	39				
28th Day.....	Cldy. Yel.	Alk.	1.032	Neg.	Neg.	Phosphates.....	40	22	8	7	4	3	6	3	93	36				
28th Day.....	Cldy. Yel.	Alk.	1.032	Neg.	Neg.	W.B.C., E.C.	40	30	11	4	4	3	7	2.5	101.5	54				

Table I.—Detailed studies of the function of a single kidney following trauma of moderate severity. (From Powers: New York State J. Med. 36: 1, 1936.)

The contused and bleeding organ was then replaced and the wound closed in layers with fine silk.

The function of this single traumatized kidney was studied daily for four days, again on the sixth, eighth, tenth, and fourteenth postoperative days, at the end of three weeks, and finally at the expiration of one month.

**Results.**—Six animals were included in this series. Three of them, in which the kidney was subjected to trauma of moderate severity, survived. The detailed studies of one animal are presented in Table I. The determinations before and after removal of the right kidney represent the average of two or more observations; those after contusion of the left kidney are single determinations.

											P.S.P. Test											
Urinalysis											Minutes											
Determination	Color	Reac-	Sp. gr.	Alb.	Sug.	Sediment	10	20	30	40	50	60	90	120	Total	N.P.N.						
Normal Control.	Cldy. Yel.	Alk.	1.026	Neg.	Neg.	Phosphates.....	12	45	20	7	3.5	3	3	3	96	5	37					
RIGHT NEPHRECTOMY																						
Normal L. Kid.	Cldy. Yel.	Alk.	1.040	Neg.	Neg.	Phosphates.....	36	22	15	7	5	3	5	3	96		40					
OPERATIVE CONTUSION OF LEFT KIDNEY																						
1st P. O. Day..	Bloody	Neut.	1.016	V.H.T.	Pos.	Loaded R.B.C.	0.5	0.5	0.2	0.3	0	0	1.5	0.5	3.5		173					
2nd Day.....	Clear Yel.	Acid	1.010	H.T.	Neg.	R.B.C., W.B.C., E.C.																
3rd Day.....	Dead					C.....	1.0	0.7	0.7	1.0	0.7	0.5	2	1.7	8	3	240					

Table II.—Detailed studies of the function of a single kidney following severe contusion and extensive trauma. (From Powers: New York State J. Med. 36: 1, 1936.)

thirteen blows with the pestle. All the studies were repeated on the first, second, fourth, and eighth days after injury. On the eighth day the normal right kidney was removed. The function of the remaining damaged organ was determined at regular intervals thereafter for one month.

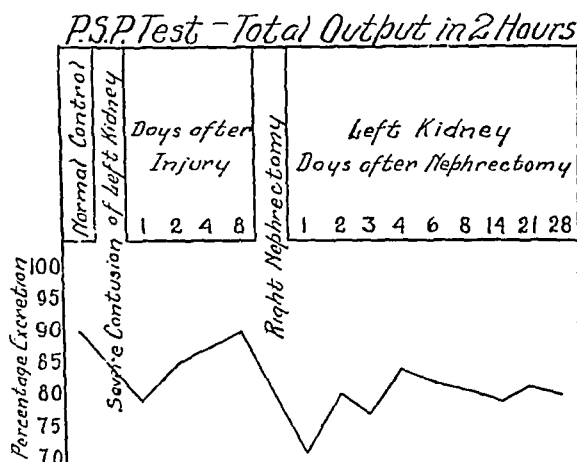


Fig. 3.—Composite curve illustrating the effect of severe unilateral renal trauma on the excretion of phenolsulphonphthalein by normal rabbits; subsequent removal of the uninjured kidney is followed by no significant impairment.

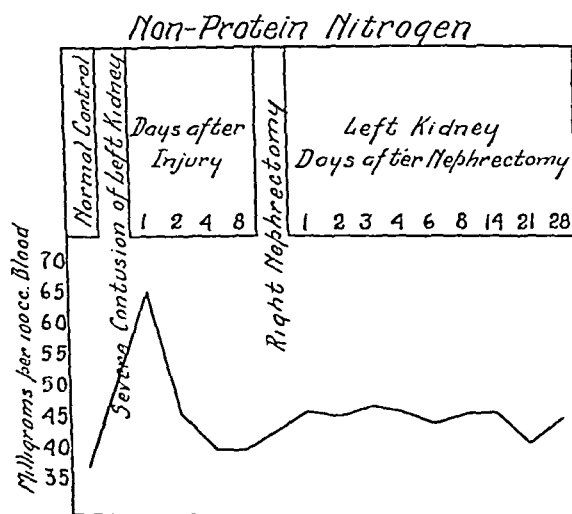


Fig. 4.—Composite curve illustrating temporary nitrogenous retention after extensive injury of one kidney of normal rabbits.

*Results.*—Nine rabbits were included in the second group of experiments. Two died within twenty-four hours after contusion of the kidney; in each case autopsy revealed extreme distention of the small intestine. Two animals died on the third day, one with pneumonia and one because of persistent, profuse hematuria. One rabbit sustained

Sudden, severe, and extensive trauma is incompatible with life if the opposite kidney has been removed.

### SECOND SERIES

The fatal outcome in the three nephrectomized rabbits whose single kidney was severely traumatized led to the further study of the effect

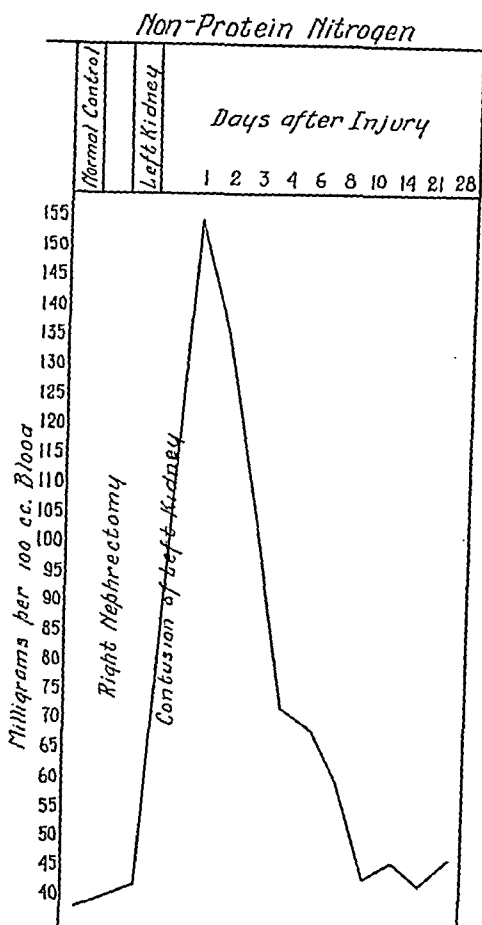


Fig. 2.—Composite curve illustrating temporary nitrogenous retention following renal trauma in rabbits previously subjected to unilateral nephrectomy. (From Powers: New York State J. Med. 36: 1, 1936.)

of extensive unilateral renal injury in rabbits with both kidneys intact. After the immediate post-traumatic period had been safely passed, the undamaged kidney was removed, leaving the animal only the seriously injured organ for the subsequent maintenance of renal activity.

*Method.*—The preliminary studies were similar to those in the first series. The left kidney was then extensively traumatized by seven to

thirteen blows with the pestle. All the studies were repeated on the first, second, fourth, and eighth days after injury. On the eighth day the normal right kidney was removed. The function of the remaining damaged organ was determined at regular intervals thereafter for one month.

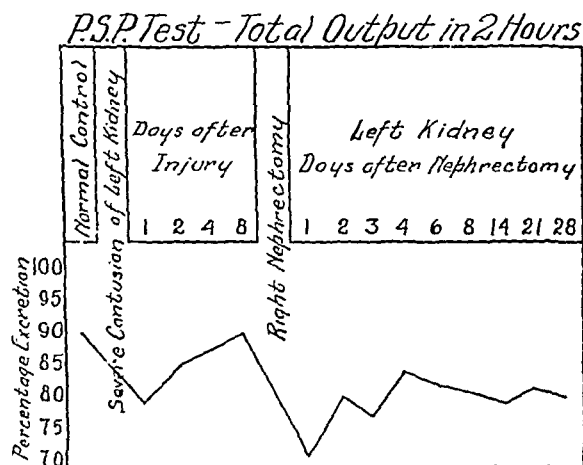


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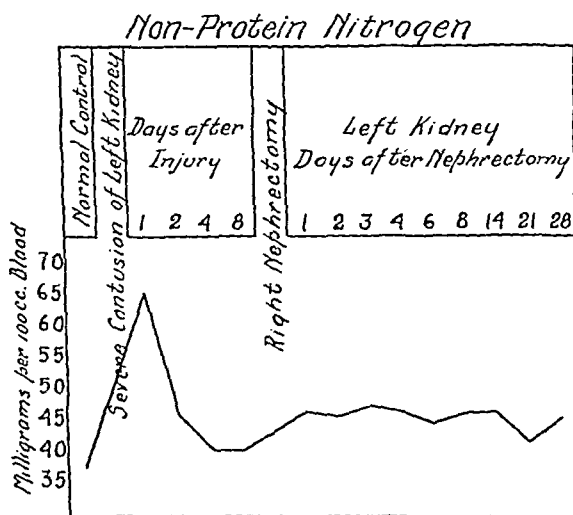


Fig. 4.—Composite curve illustrating temporary nitrogenous retention after extensive injury of one kidney of normal rabbits.

*Results.*—Nine rabbits were included in the second group of experiments. Two died within twenty-four hours after contusion of the kidney; in each case autopsy revealed extreme distention of the small intestine. Two animals died on the third day, one with pneumonia and one because of persistent, profuse hematuria. One rabbit sustained

## RABBIT No. 190

RABBIT NO. 190										P.S.P. Test									
Determination	Color	Reaction	Urinalysis			Sediment	Minutes										Total N.P.N.		
			Sp. gr.	Alb.	Sug.		10	20	30	40	50	60	90	120					
Normal Control	Cldy. Yel.	Alk.	1.042	Neg.	Neg.	Phosphates	40	25	9	6	3	2	2	3	90	41			
OPERATIVE CONTUSION OF LEFT KIDNEY																			
1st P. O. Day	Cl. Yellow	Acid	1.010	T.	Neg.	R.B.C., W.B.C., E.C.	25	15	10	6	3.5	3	6	3	71.5	100			
2nd Day		No Urine Obtained					18	17	13	8	6	6	6	6	80	75			
4th Day	Cldy. Yel.	Alk.	1.028	Neg.	Neg.	Rare W.B.C.	32	15	12	7	6	3.5	5	3.5	84	46			
8th Day	Cldy. Yel.	Alk.		Neg.	Neg.	Phosphates	15	35	15	7	7	2.5	7	2	90.5	46			
RIGHT NEPHRECTOMY																			
1st P. O. Day	Cl. Yellow	Acid		Neg.	Neg.	Few W.B.C.	18	10	8	6	4	4.5	7	4.5	62	60			
2nd Day	Cl. Yellow	Alk.		Neg.	Neg.	Rare W.B.C.	18	15	8	6	7	4	7	5	70	60			
3rd Day	Cldy. Yel.	Alk.	1.035	Neg.	Neg.	Few W.B.C.	15	18	10	8	4	5	7	4	71	41			
4th Day	Cldy. Yel.	Alk.	1.028	S.P.T.	Neg.	Few W.B.C.	20	15	7	6	6	5	10	5	74	54			
6th Day	Cldy. Yel.	Alk.	1.033	Neg.	Neg.	Carbonates	16	20	7	8	5	4	11	5	76	48			
8th Day	Cldy. Yel.	Alk.	1.035	Neg.	Neg.	Carbonates	15	18	15	7	7	3.5	10	5	80.5	48			
14th Day	Cldy. Yel.	Alk.		Neg.	Neg.	Phosphates	20	15	10	6	6	4	8	6	75	60			
21st Day	Cldy. Yel.	Alk.		Neg.	Neg.	Carbonates	20	15	12	5	5	5	9	4	75	44			
28th Day	Cldy. Yel.	Alk.	1.019	S.P.T.	Neg.	W.B.C., E.C.	23	17	10	7	5	4	8	4	78	44			

Table III.—Detailed studies of renal function following severe unilateral trauma in a rabbit with the opposite kidney intact.

the trauma satisfactorily but died from acute hemorrhage on the day following removal of the uninjured kidney.

The data from the four remaining rabbits are presented graphically in Figs. 3 and 4 for comparison with the first series of experiments, and the detailed studies of one animal are tabulated in Table III. From a study of these figures it is apparent that severe trauma of one kidney of a normal animal may cause only a transient and slight drop in the total excretion of phenolsulphonaphthalein or rise in the nonprotein nitrogen of the blood. Following removal of the uninjured kidney, the impairment of renal function is slight.

*Conclusion.*—If severe injury is inflicted upon one kidney of a normal rabbit, the renal function may be maintained quite satisfactorily by the opposite kidney, with no significant impairment during the immediate convalescent period. If this normal organ is then removed, the traumatized kidney may recover sufficient function to continue the maintenance of renal activity at a satisfactory level thereafter.

## STRUCTURAL CHANGES SECONDARY TO TRAUMA

*Gross Anatomic Changes.*—Direct trauma of moderate severity (four or five smart raps with the pestle) produced immediate swelling, diffuse subcapsular hemorrhage, capsular tears, and small cortical lacerations on both the anterior and posterior surfaces of the kidney. Severe trauma (seven to twelve blows) caused extensive hemorrhage, ragged wounds of the parenchyma communicating with the pelvis (Fig. 5) and frequently complete decapsulation. The kidney became reddish black in color, soft, pulpy, and lifeless in consistency.

Fig. 6 illustrates the kidney of an animal which was killed on the second day after contusion. The perirenal tissues and overlying peritoneum were edematous and hemorrhagic; the capsule was separated except at the pelvis, shrivelled up, and adherent to the anterior surface

of the kidney. Large, irregular, yellowish gray plaques were apparent superficially and, on section, were found to extend into the cortex for a distance of 1 or more mm. Several clots of blood were found in the pelvis; the mucosa was ruptured in places, and radiating out fan-wise through the medulla were areas of gross hemorrhage.

The return of renal function after injuries of comparable extent and severity was striking.

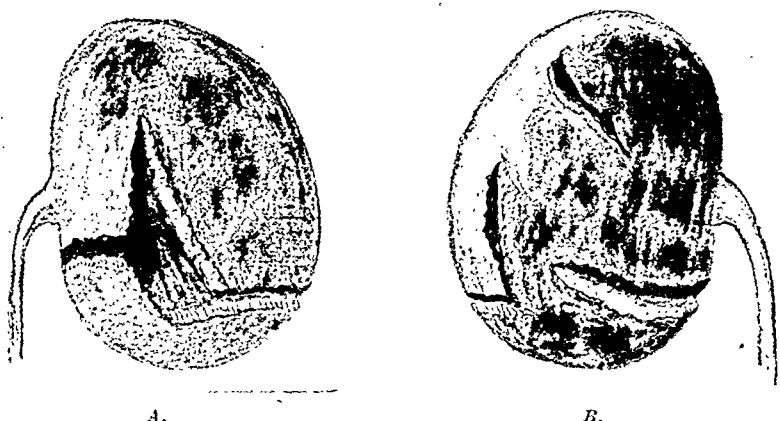


Fig. 5.—Operative sketch illustrating the effect upon the kidney of severe experimental trauma. A, Anterior aspect; B, posterior aspect. (From Powers: New York State J. Med. 36: 1, 1936.)

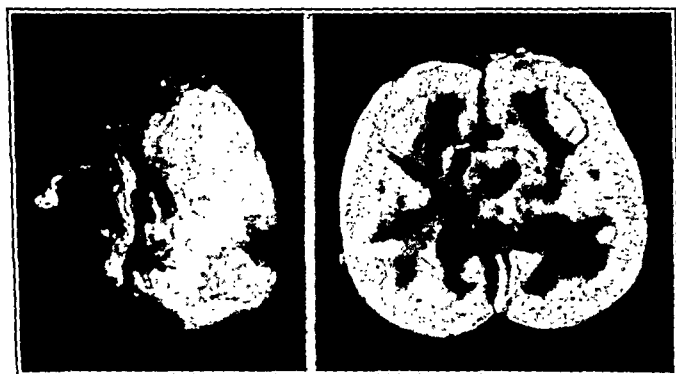


Fig. 6.—Photographs of a kidney removed on the second day after extensive injury. The capsule is attached only at the pelvis; large superficial yellowish-gray plaques and extensive parenchymal hemorrhage are apparent.

*Microscopic Changes.*—The early histologic changes following injury of moderate severity were those of tubular degeneration with relatively little damage to the glomeruli, greatly swollen and congested vessels, extravasation of blood, cortical hemorrhage continuous with that beneath the capsule, and areas of infarction with complete necrosis of the tubules and infiltration of polymorphonuclear leucocytes (Fig. 7). In



many places the tubules were plugged with hyaline and cellular casts. Mitotic figures were abundant, indicating rapid regeneration of tubular epithelium (Fig. 8).

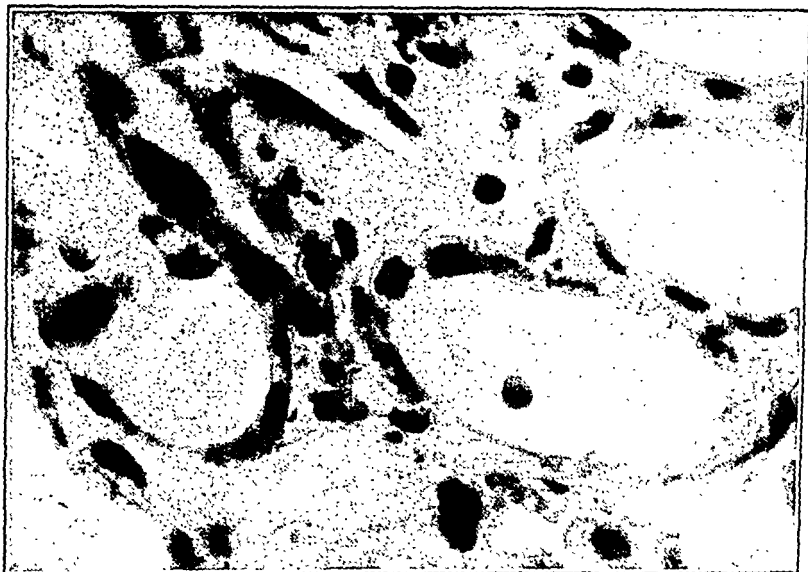


Fig. 8.

Fig. 7.—Photomicrograph of renal infarct showing tubular degeneration and leucocytic infiltration in the infarcted area ( $\times 150$ ).  
Fig. 8.—Photomicrograph of mitotic figure in tubular epithelial cell ( $\times 1250$ ).



Fig. 7.

Complete destruction of large areas of renal tissue followed trauma of greater severity. Outside these were zones of infiltration with inflammatory cells. Adjacent were areas in which both the degenerating tubules and casts contained large amounts of calcium (Fig. 9). The

histologic picture is not dissimilar to that which is found in poisoning with corrosive sublimate.

Healing occurred by the formation of scar tissue which, in some sections, was very dense, completely replacing all functioning renal tissue. Little blood pigment was left in places of former hemorrhage. No casts were apparent and the changes which remained were those of distortion and cicatrization.



Fig. 9.—Deposits of calcium in degenerating tubules and casts ( $\times 150$ ).

#### CONCLUSION

Impairment of renal function following trauma of moderate severity is transient. Severe injury is incompatible with life if the opposite kidney has been removed. Extensive trauma to one kidney, if the other organ is intact, may cause no great change in total renal function. If the undamaged kidney is subsequently removed, the injured organ will regain sufficient function to maintain renal activity at a satisfactory level.

The chief pathologic changes responsible for the transient impairment of function following injury are degeneration of the tubules,

subcapsular and parenchymatous hemorrhage, edema, and infarction. Prompt functional recovery is due to the rapid regeneration of tubular epithelium.

The results suggest that the majority of patients with unilateral renal trauma may be treated conservatively with the expectation that the injured kidney will recover sufficient function to be a useful and serviceable organ.

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# NEWER CONCEPTS IN THE TREATMENT OF INJURIES TO THE LIGAMENTS OF THE KNEE JOINT: AN EVALUATION OF THE MAUCK OPERATION

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THE fact, as noted by Jones and Smith,<sup>1</sup> that stable knees may follow severe dislocations of the knee joint treated conservatively; the practice of some surgeons to disregard or excise torn crucial ligaments with satisfactory stable results; and the more recent contributions of several observers who, in the presence of collateral and crucial ligament injuries, have secured stable knees by the repair of the former alone, have strongly suggested the minor rôle played by the crucial ligaments in the integrity and function of the knee joint and, therefore, the lack of need in most cases for severe reconstructive procedures of the Hey-Groves<sup>2</sup> type.

It is our intent (1) to express clinical and experimental confirmation of the above observations, and (2) to emphasize the applicability of the Mauck<sup>3</sup> operation, not only in the treatment of a relaxed internal lateral ligament, but also for the restoration of stability and normal function in a knee joint with associated injuries to the crucial and collateral ligaments.

## ANATOMIC CONSIDERATIONS

The tibial collateral (internal lateral) ligament is attached to the medial condyle of the femur, near the adductor tubercle; it crosses the medial aspect of the joint where it becomes attached to the peripheral border of the internal meniscus and is inserted into the medial border of the tibia, behind the semitendinosus tendon. It consists of a long superficial and a short deep portion, and it is the latter which shares the intimate relation with the internal semilunar cartilage.

The fibular collateral (external lateral) ligament is a distinctly palpable, rounded band attached to the lateral femoral epicondyle; it is separated from the lateral aspect of the knee joint by the popliteus tendon and its bursa. At its insertion to the fibular head, the two slips of attachment of the biceps tendon with an interposed bursa embrace it.

The anterior crucial (cruciate) ligament, attached above to the outer femoral condyle far back in the intercondylar notch, is directed downward, forward, and a little inward to its attachment in front of the tibial spine.

## SURGERY

subcapsular and parenchymatous hemorrhage, edema, and infarction. Prompt functional recovery is due to the rapid regeneration of tubular epithelium.

The results suggest that the majority of patients with unilateral renal trauma may be treated conservatively with the expectation that the injured kidney will recover sufficient function to be a useful and serviceable organ.

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1. Powers, John H.: Renal Function Following Trauma of the Kidney; a Clinical and Experimental Study. *New York State J. Med.* 36: 1-7, 1936.

Honigschmeid<sup>11</sup> noted that (1) hyperextension produced a loosening of the crucial ligament attachments, of the anterior from the tibia, and of the posterior from the femur; (2) excessive flexion tore the anterior crucial ligament from its femoral attachment; (3) excessive adduction of the leg on the thigh ruptured the external lateral ligament, the anterior crucial ligament, and then the posterior crucial ligament; (4) excessive abduction detached the internal collateral ligament, posterior crucial, and then the anterior crucial ligaments; (5) excessive internal rotation of the tibia on the femur ruptured the capsule and anterior crucial ligament; and (6) excessive external rotation of the tibia detached the posterior crucial ligament from the tibia, ruptured the anterior crucial ligament, and detached the internal meniscus.

Pringle<sup>12</sup> observed that, if through a small incision the anterior crucial ligament was divided, no abduction was possible in the extended position and only a slight degree in the flexed position, but that the range of abduction was greatly increased with section of the internal collateral ligament. He produced rupture of the anterior crucial ligament in cadavers by fixing the pelvis, flexing the knee, abducting the leg and rotating it inwards on the femur. In all cases he noted that there was concomitant tearing of the deep fibers of the internal lateral ligament.

Observations by one of us (M. T. H.) on the knees of ten cadavers at the Daniel Baugh Institute of Anatomy of the Jefferson Medical College and on fresh specimens from four large dogs serve to corroborate many of the above findings. The integrity of the knee was disturbed as little as possible through small anteromedial incisions and the necessary severance performed with a tenotome. It was noted that:

1. With the knee fully extended, section of the anterior crucial ligament, posterior crucial ligament, or both, did not disturb the stability of the knee. No undue lateral or rotatory motion and only very slight anteroposterior motion was present.

2. With the knee in full extension, the collateral ligaments severed, and the crucial ligaments intact, definite anteroposterior, lateral, and rotatory motion existed, which became greatly exaggerated with severance of the crucial ligaments.

3. With the knee flexed, if the anterior crucial ligament was severed, anteroposterior ("rocker") motion became evident; but this was greatly increased, as was also the range of abduction and rotation of the tibia on the femur with the knee flexed, when the internal collateral ligament was severed.

4. With the knee flexed, even though the anterior crucial ligament was left intact, severance of the internal lateral ligament resulted in definite "rocker" motion, with increase in abduction and rotation of the tibia on the femur.

The posterior crucial (cruciate) ligament is attached above to the front part of the inner aspect of the femoral intercondylar notch and passes downward, backward, and a little outward to become attached to the tibia at the posterior portion of its articular surface.

The integrity of the knee joint depends not only on these ligamentous structures but also upon the posterior oblique ligament, the muscular aponeuroses and tendons about the joint, and, to a less extent, the capsule and menisci.

The lateral ligaments become taut in full extension, checking hyperextension, lateral motion, and rotation. In flexion, since their femoro-tibial attachments approximate, they are relaxed; the knee joint becomes loose, and slight lateral and rotatory motion about a longitudinal axis now becomes possible (Steindler<sup>4</sup>).

The usual conception of crucial ligament function, based on its anatomic construction, is that the anterior crucial ligament, checking forward displacement of the tibia, becomes tense in full extension, while the posterior crucial ligament, checking backward displacement of the tibia, becomes taut in full flexion. Milch<sup>5</sup> notes that this is at variance with the studies of Weber,<sup>6</sup> Meyer,<sup>7</sup> and Fick,<sup>8</sup> who observed that during flexion and extension different portions of both crucial ligaments became taut in different stages of motion, and that the position of maximum tension of both crucial ligaments was that of flexion and internal rotation of the tibia on the femur. "From these considerations it appears reasonable to conclude that the crucial ligaments function mainly during the act of flexion, and that during extension the support of the knee is undertaken by other structures, viz., the collateral ligaments and the muscles about the joint" (Milch).

#### EXPERIMENTAL CONSIDERATIONS

Giertsen<sup>9</sup> quotes Hyrtl's anatomic observations that (1) in extension the stability of the knee remains intact if the crucial ligaments are severed, provided that the collateral ligaments remain intact; and (2) instability in flexion and extension results if the collateral ligaments are severed and the crucials left intact.

Weber,<sup>6</sup> as noted by Milch, observed that with the collateral ligaments intact and the crucial ligaments severed, the knee was stable in extension and unstable in flexion, while the reverse conditions existed if the collateral ligaments were sectioned and the crucials preserved.

Pagenstecher<sup>10</sup> ruptured the anterior crucial ligament in cadavers by blows from behind applied to the upper end of the tibia with the knee flexed, and the posterior crucial ligament by blows upon the front of the upper tibial extremity. He could rupture the anterior crucial ligament only at its femoral attachment.

relaxed anterior crucial ligaments and each with a positive "rocker" sign and lateral instability, secured stable knees by employing his method of internal lateral ligament reinforcement.

#### TREATMENT

Injury, either as actual tears or stretching, to the internal collateral ligament should be anticipated in all injuries of the knee joint. Secondary relaxation may follow uncontrolled intraarticular effusion. Conservative therapy is indicated in the early stages, with aspiration deferred until forty-eight hours after the injury is incurred and then repeated if necessary. Immobilization is best secured with a close-fitting plaster bandage, and in injuries of the collateral ligaments alone this may be hinged at the knee to allow flexion and extension and yet inhibit lateral stress and torsion.

For the surgical reconstruction of the internal lateral ligament, Alwyn Smith<sup>13</sup> utilizes the additional length of the fascial strip employed to reconstruct the anterior crucial ligament, to bridge the medial aspect of the knee joint, suturing it to the internal femoral condyle. Bennett<sup>17</sup> plicates the relaxed internal capsule, reinforcing this in his more recent cases with fascial strips. Cotton and Morrison<sup>21</sup> and Bosworth and Bosworth<sup>23</sup> employ a fascial strip, run through drill holes on the medial surfaces of the inner femoral and tibial condyles and made to bridge the joint in cross-fashion. Wilson<sup>28</sup> and Campbell<sup>29</sup> use a pedunculated fascial flap, its femoral attachment preserved, suturing it to the medial surface of the internal tibial condyle. Others prefer the use of adjacent tendons to reinforce the internal ligament; McMurray<sup>30</sup> utilizing the sartorius; Eikenbary,<sup>15</sup> the semitendinosus; Edwards,<sup>31</sup> the gracilis and semitendinosus; and Phillips,<sup>32</sup> the gracilis alone.

Mauck<sup>3</sup> described his procedure for the treatment of relaxation of the internal lateral ligament following trauma and effusion and unrelieved by a conservative regime. He attributes such relaxation to detachment of the internal lateral ligament with its attached internal semilunar cartilage from its tibial insertion. The resulting hypermobility is often aggravated by the removal of the internal meniscus, deranged or benign, and such a knee is predestined for further derangement. His procedure is performed as follows:

The inner aspect of the knee joint is exposed through a slightly anterior curved incision, extending from the adductor tubercle of the femur to 4 inches below the joint line, and the skin and fascia are dissected anteriorly and posteriorly. With a broad chisel the inner side of the tibial head, with the attached internal lateral ligament, is removed and reflected upwards, this triangular-shaped flap measuring  $1\frac{1}{2}$  inches in length and  $\frac{1}{2}$  inch in thickness at the articular surface. The capsule is incised at the anterior and posterior margins of the bony flap, and the internal meniscus, attached to the capsular flap, is excised.



5. In two cadavers, with the pelvis fixed and the knee flexed, the leg was forcefully abducted on the femur. The internal lateral ligament was torn from its tibial attachment in each case, and with the abducting force continued, marked stress was placed upon both crucial ligaments, the greatest strain being exerted on the anterior when the leg was internally rotated and on the posterior when the leg was externally rotated. In this position the internal meniscus, its anterior and posterior attachments intact, became displaced into the knee joint, but no actual tear was seen to occur, possibly due to the absence of superincumbent weight.

#### CLINICAL CONSIDERATIONS

These anatomic studies serve to confirm the clinical experience of a small group of observers.<sup>13-26</sup> Their contentions are well expressed in the conclusion of Milch's<sup>5</sup> excellent paper: "I have come to believe that, contrary to general opinion, the anterior crucial ligament is not a vitally necessary structure and that its loss is thoroughly compatible with relatively normal function of the knee, that the diagnosis of rupture of this ligament alone is not as simple as it has been stated to be, that the tests ('rocker' and extension tests) are in all probability indicative of injuries to both the crucial and the internal lateral ligaments, that the disability is due primarily to the loss of integrity of the internal lateral ligament, and that in consequence surgical efforts should be directed primarily toward the repair of the internal lateral ligament . . . rather than repair of the crucial ligament. . . ."

The great improvement in the results of crucial ligament repair with fascia or tendon by the Alwyn Smith<sup>13</sup> modification, of additional reconstruction of the internal lateral ligament, was immediately appreciated and accepted by Hey-Groves<sup>27</sup> and utilized by later contributors. Bennett<sup>17</sup> successfully treated five out of six cases with torn anterior crucial ligaments confirmed by arthrotomy by his method of plication of the medial capsule and fascial reenforcement of the internal lateral ligament alone, with resulting normal stability and function. Cotton and Morrison,<sup>21</sup> and Bosworth and Bosworth<sup>23</sup> secured stable knees with their methods of internal lateral ligament reconstruction, disregarding the repair of the associated torn anterior crucial ligaments. Tixier and DeRougemont<sup>24</sup> excised a fractured tibial spine and the entire anterior crucial ligament with resulting excellent stability and knee function, confirming similar experiences by Tavernier,<sup>14</sup> Leriche and De Girardier,<sup>16</sup> and Constantini and Coniot.<sup>25</sup> In discussing this paper Tavernier<sup>26</sup> reported a case of anterior crucial and internal lateral ligament tears, wherein restoration of the latter alone resulted in a normal knee. Milch,<sup>5</sup> also, has noted satisfactory knee-joint stability following the resection of a torn anterior crucial ligament. Most recently, Mauck,<sup>3</sup> in three cases, one with demonstrable tear and two with

## CASE REPORTS

CASE 1.—W. L., a colored male, aged twenty years, injured his left knee in a fall one year prior to admission, with resulting persistent disability and instability. On examination the left knee evidenced periarticular swelling and a moderate synovial effusion. The range of motion was from full extension to a right angle. There was definitely localized tenderness in the region of the anterior attachment of the internal meniscus. With the knee fully extended, definite anteroposterior motion of the tibia on the femur was elicited and the leg could be abducted  $15^{\circ}$  to  $20^{\circ}$ . With the knee flexed, the "rocker" sign was strongly positive. Roentgenographic studies of the affected knee and all laboratory studies were negative.

A preoperative diagnosis of torn anterior crucial ligament, torn internal meniscus, and relaxed internal collateral ligament was confirmed at the time of operation (Feb. 3, 1937), at which time the Mauck procedure was performed. The extremity was immobilized in a plaster bandage for two weeks and hinged at the knee for four additional weeks.

Restoration of function was rapid with complete return of motion six weeks following the removal of the plaster. All anteroposterior and abnormal lateral motion had disappeared. To date there has been no secondary relaxation and the patient has returned to his vocation of bell-hop.

CASE 2.—L. K., a white male student, aged eighteen years, injured his left knee one year prior to admission while playing ball. He thereafter suffered persistent pain, swelling, weakness, and instability. Examination revealed the left knee to be moderately swollen due to a synovial effusion and thickened synovial membrane. There was localized tenderness at the anterior horn of the internal semilunar cartilage and in the region of the tibial attachment of the internal lateral ligament. There was undue anteroposterior and lateral motion of the tibia on the femur with the knee fully extended and a positive "rocker" sign with the knee flexed. The range of motion was normal. X-ray studies of the injured knee were negative.

A preoperative diagnosis of torn anterior crucial ligament, torn internal meniscus, and relaxed internal collateral ligament was confirmed at operation (June 20, 1937), at which time a typical Mauck procedure was performed. The knee was completely immobilized in plaster bandage, in full extension, for three weeks.

Normal function returned rapidly following the removal of fixation. The abnormal anteroposterior and lateral movements were no longer evident and the "rocker" sign was barely elicited. There has been no secondary relaxation up to the present.

In two other cases with disruption of the anterior crucial ligament, corroborated at the time of arthrotomy for deranged internal menisci, but with intact internal lateral ligaments, excellent stability without any preternatural mobility resulted, although the crucial ligament tears were disregarded. One other case is significant, a severe, traumatic, medial dislocation of the tibia on the femur with unquestionable severance of both crucial ligaments. Conservative treatment was instituted and the extremity encased in a plaster bandage, with resulting excellent stability and normal function. We feel that in this case the internal collateral ligament was not critically ruptured and possibly only severely stretched.

## CONCLUSIONS

1. A review is given of previous experimental and clinical observations and our own contributions are described to substantiate the con-

The knee joint may now be thoroughly inspected. To shorten the internal lateral ligament, the bone flap is pulled downwards forcefully, and with the leg fully extended and strongly adducted it is mortised into a trough prepared  $\frac{3}{4}$  to  $1\frac{1}{4}$  inches below its former site, on the medial aspect of the tibia. Thus the lower end of the ligament, i.e., its weakened fibrous portion, contacts a fresh bony surface to which it becomes adherent (Fig. 1 A and B). The capsule is plicated if necessary and the subcutaneous tissue and skin closed. Mauck then applies a plaster bandage with the knee in full extension for six weeks, and this is hinged at the knee at the end of two weeks to allow early flexion and extension.\*

This technique has been employed by the senior author (A. J. D.) in the treatment of two cases, each with proved anterior crucial ligament tear, torn internal meniscus, and marked relaxation of the internal

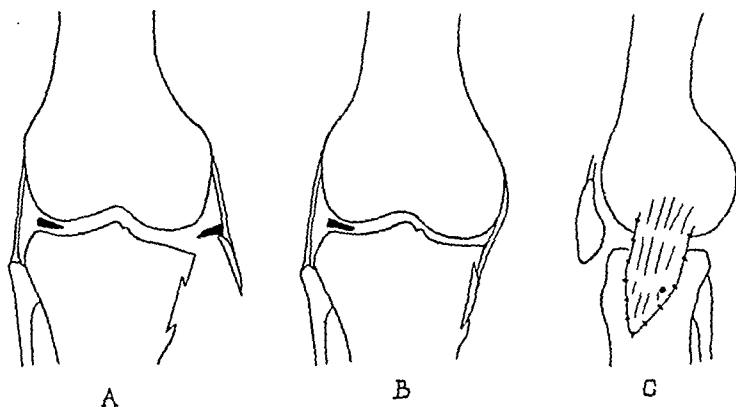


Fig. 1.—Illustrating the Mauck operation. A, The tibial bone flap and its attached internal lateral ligament reflected upwards, and a trough constructed on the medial tibial surface; B and C, the bone flap displaced downwards and forwards under tension and mortised into place following removal of the internal semilunar cartilage.

collateral ligament. The whole bone flap was implanted forward as well as downward to increase the obliquity of the anterior fibers of the ligament and to act as an additional check against forward movement of the tibial head on the femur, as recommended but not practiced by Mauck (Fig. 1 C). The procedure seems most applicable for this type of case because it permits an excellent exposure of the interior of the knee joint without unduly disturbing its capsuloligamentous envelope; because the removal of the internal meniscus, deranged or normal, permits a close approximation of the tibia to the femur; and because it is a direct attack upon and actual shortening of the internal lateral ligament rather than a substitution by fascia or tendon.

\*Wittek, A. (Zur Wiederherstellungs-Chirurgie des Kniegelenkes, Wien. klin. Wchnschr. 50: 803, 1937) describes an exposure of the knee joint not unlike the Mauck operation. He chisels off a portion of the medial femoral epicondyle, turning it down with a portion of the capsule, and, following repair of the internal structures, nailing the separated epicondyle into a new bed proximal to its original position, under tension.

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cept that the anterior crucial ligament is not vital to the integrity of knee joint stability and function; that the diagnostic signs usually described as indicative of crucial ligament injury are also indicative of internal collateral ligament derangement; and that surgical procedures should seek to correct the relaxed or torn internal lateral ligament alone.

2. The Mauck procedure is described and its value in the correction of relaxation of the internal lateral ligament is corroborated.

3. The adaptability of the Mauck technique for the repair of the relaxed internal lateral ligament associated with tear of the anterior crucial ligament is stressed. Where the internal ligament is frankly and irreparably ruptured, a fascial or tendinous reconstruction becomes obligatory.

We are deeply grateful to Professor J. Parsons Schneffler, Director of the Daniel Baugh Institute of Anatomy, Jefferson Medical College, for the liberal supply of anatomic material.

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## POSTERIOR DISLOCATION OF THE FIRST CERVICAL VERTEBRA WITH FRACTURE OF THE ODONTOID PROCESS

RUDOLPH S. REICH, M.D., CLEVELAND, OHIO

THE incidence of dislocation of the upper cervical spine associated with fracture is not rare. In fact, the literature abounds in numerous reports of the condition. In looking through the literature, however, one is impressed with the absence of posterior dislocation of the first cervical vertebra and the treatment of this apparently unusual injury. This is the reason for reporting the single case, the report which is as follows:

CASE REPORT.—Mrs. L. M., aged fifty-five years, was riding in the front seat of an automobile next to the driver on Oct. 27, 1934, when she was thrown out of her seat in a head-on collision, her forehead striking the sill above the windshield and her head being thrust forcibly backward. She immediately sensed increasing difficulty in using her arms and was helpless when she arrived in the hospital. She states that she was numb from her neck down; and whereas she had some control of her arms and legs, she was unable to regulate these movements, which were more or less purposeless. She sustained a very extensive scalp wound involving almost the entire frontal and biparietal areas. Her scalp wound was sutured and she was placed in bed with sandbags on either side of her head.

She was seen by me in consultation ten days after the accident. At this time, examination revealed an extensive suppurating scalp wound involving the frontal and biparietal regions. The chin was pointed upward and to the right. There was complete limitation in rotation of the head, and the other movements of the cervical spine were markedly restricted. The pronator, biceps, triceps, patellar, and Achilles reflexes were all present and symmetrical, but markedly increased, slightly more on the left side. She stated that since her accident she had noticed a slight improvement of her right arm, so that at the time of my first examination she was able to grasp an object on the bedside table next to her. The left arm, however, was "still entirely out of control." She was able to move her lower extremities and there was no sensory disturbance. There was no urinary or fecal incontinence.

Roentgenograms (Figs. 1 and 2) taken immediately after the accident showed the first cervical vertebra to be dislocated posteriorly for a distance of approximately  $\frac{1}{8}$  inch, and to the left side for a distance of approximately  $\frac{1}{4}$  inch. Obviously, the articular facets were also dislocated and there was a fracture of the odontoid process which was displaced posteriorly.

The patient was removed to Mt. Sinai Hospital, Cleveland, Ohio, where reduction was attempted as follows: The patient was given preliminary hypodermic injection of morphine sulphate, gr. 1/6, and atropine sulphate, gr. 1/150, followed by tribromethanol anesthesia, 80 mg. per kilogram of body weight. She was then placed on the Albee fracture table and reduction was accomplished by reversing the Walton maneuver. In other words, the patient was placed supine instead of prone on the fracture table and a halter was applied and fixed to a web strap which was placed around my waist. Because of the necessity of obtaining an upward pull, it was necessary to be elevated on a stool, approximately eighteen inches high. By

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means of constant pull obliquely upward, the head was turned first to the left side, and then to the right. There was no click as frequently occurs in anterior dislocation.



Fig. 2.



Fig. 1.

Fig. 1.—Lateral view showing posterior dislocation of the first cervical vertebra on the second, with fracture of the odontoid process displaced posteriorly.  
Fig. 2.—Anteroposterior view showing dislocation of the articular processes between the first and second cervical vertebrae to the left.

tions; in fact, there was no sensation whatever of a reduction. The head was maintained in this position until another roentgenogram was obtained by a portable unit. This showed a complete reduction as illustrated in Figs. 3 and 4. In this



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position, a plaster of Paris bandage was applied, including the upper torso, shoulders, neck, and head, cutting out a window for dressing the scalp wound, and the patient was placed in bed.

Within three days she began to note improvement of the sensory function of her left arm, and after approximately ten days, the motor control of the left arm became evident, although the movements at that time were still incoordinated. However, within approximately another two weeks the patient was able to reach for articles and grasp them, and from then on motor recovery continued to improve. About two months after reduction, she was able to feed herself. Four weeks following the reduction and application of the cast, it was removed and another plaster bandage applied, which now included the entire scalp, as the scalp wounds had healed. This remained applied for approximately three and one-half weeks, when it was removed and replaced by another. This bandage remained applied for six weeks, after which period it was removed and an aluminum neck brace applied. This brace was removed periodically and active rotation encouraged.

Three months following the reduction, the patient was able to get about without any difficulty whatever and had complete control of her right arm, although she still complained of some "weakness" in her left. This weakness did not impair her from using it for the usual necessities. The reflexes of the arm and forearm had diminished in intensity and were now symmetrical. In spite of the fact that the patient had no difficulty with the lower extremities, the patellar reflexes continued to be slightly exaggerated up to the last examination, Dec. 17, 1936.

After six months the brace was entirely discarded and more active rotation encouraged. Rotation is now approximately 75 per cent of normal, and the other movements are not impaired.

#### COMMENT

1. Search of the literature reveals that many cases of dislocation of the first cervical vertebra associated with fracture have been reported, but these cases are all anterior dislocations. Brooks' various articles are probably the most comprehensive, notably, the one published in 1933 which reports forty cases, of which twenty were fractures of the first cervical, every one being an anterior dislocation. These anterior dislocations present a very definite deformity; namely, the head tilted forward, with the chin on the upper thorax in some instances. In the posterior dislocation, the head is obviously in the opposite position, being tilted backward with the head a little to one side and the chin pointing upward.

2. It is interesting to note that the Walton maneuver also may be applied to the posterior type of dislocation, with position of the patient and the maneuver naturally reversed. This type of maneuver has been very successful in this case.

3. I have been particularly gratified with the use of rectal anesthesia in this case, as it worked perfectly. The patient was always under control, and we did not experience any inconvenience at having the anesthetist in our way, which would necessarily be the case in inhalative anesthesia. This method also has been used numerous times by the writer in reducing compression fractures of the spine.



Fig. 3.—Lateral view showing reduction of dislocation of the first cervical vertebra and alignment of the fractured odontoid process.



Fig. 4.—Anteroposterior view showing reduction of the laterally dislocated articular processes. The odontoid process is seen fractured at its base.

## RECTOVAGINAL CLOACA

### REPORT OF A CASE AND A SIMPLE METHOD OF RECONSTRUCTION

CHARLES W. MAYO, M.D., AND WINFIELD L. BUTSCH, M.D.\*  
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*(From the Division of Surgery, the Mayo Clinic, and the Mayo Foundation)*

SINCE Bodenhamer's definitive volume on congenital malformations of the rectum and anus, which was written in 1860, there have been few published instances of the surgical treatment of rectovaginal cloaca. A notable exception to this was the description by Stone of his operation for this defect in 1936. His procedure is suited for the cases in which the rectum opens into the posterior wall of the vagina at a variable distance above the vaginal introitus. In our case the rectum opened into the vagina at the posterior fourchet. This, according to Stone, is the commonest type of rectovaginal cloaca. It seemed advisable, therefore, to report the case in which we recently performed an operation by a simple method and in which the result was successful.

From the standpoint of comparative anatomy, the cases reported by Stone represent an arrest at an earlier stage in the evolutionary scale than does our case. In amphibia the rectum opens into the top of the cloaca, which would correspond to an opening of the rectum into the posterior fornix of the vagina of the malformed human female. The opening of the rectum passes downward as one ascends the evolutionary scale to the reptilia, in which it opens midway down the cloaca. In marsupials the rectum opens into a very small cloaca very near the perineum. This corresponds to the condition obtaining in our case.

Sir Arthur Keith said that these malformations occur in one of about every 5,000 infants so it may be beyond the experience of any one physician to encounter the condition. Yet, if the condition is encountered, one should know a safe and successful method of treatment. It is the consensus that operative treatment should not be instituted until the child reaches the age of at least six or seven years. Spontaneous separation of the rectum and vagina has occurred when operation has been thus postponed. Dilation of the vaginal orifice of the rectum is usually sufficient, as a temporary expedient, to permit the patient to have unimpeded bowel movements until operation is deemed advisable.

Lynch and Hamilton have recently described congenital abnormalities of the rectum and suggested operative procedures for their correction.

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\*Fellow in Surgery, the Mayo Foundation.

## SUMMARY

A case of posterior dislocation of the first cervical vertebra associated with fracture and also with fracture of the odontoid process of the second cervical vertebra is reported. The Walton method of reduction, reversing the position of the patient and reversing the maneuver, proved very successful. Rectal anesthesia, by the employment of tribromethanol, offered complete relaxation without the inconvenience of having an anesthetist in one's way.

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## REPORT OF CASE

A girl, aged eleven years, was brought to the clinic because her "rectum was not in the right place." Shortly after her birth her parents had noted that the rectum opened into the same cavity as did the vagina. The opening was small and feces had to be extracted manually on numerous occasions. When she was one year old her physician had dilated the opening of the rectum and this had facilitated her bowel movements considerably. However, she had continued to depend on the frequent use of cathartics and enemas. Three years before her admission to the clinic she had been advised to take mineral oil daily, which had aided in the expulsion of feces. During the year before the patient came to the clinic her sphincteric control had been poor and there had been daily soiling of her clothes.

The urethral orifice was normal and the vagina was well developed. The lower half of the rectovaginal septum was entirely lacking. The rectum communicated with the vagina at this point. The fourchet had been replaced by the posterior rectal wall. The anterior half of the external and sphincter was absent, but a semicircular posterior portion was palpable and partially surrounded the posterior rectal wall.

Proctoscopic examination revealed that the rectum and sigmoid colon were dilated to two or three times their normal diameter throughout the distal 24 cm. A barium enema was given, but the roentgenogram of the colon was unsatisfactory because of the patient's inability to retain the enema. However, the roentgenologist did not find any evidence of a megacolon.

The operative method used was an adaptation of the commonly used means of restoring the perineal body following laceration caused by childbirth. In this instance it has served very well to construct the perineal body of a girl who had never had one. Fig. 1 *a* shows the condition of the patient when she presented herself for examination. The posterior half of the external sphincter of the anus was present and could be palpated. By parting the labia, the upper part of the incomplete rectovaginal septum could be seen (Fig. 1 *b*). This was pulled down with tenaculum forceps and an incision was made in its free border (Fig. 1 *c*). The vaginal and rectal mucous membranes were then carefully dissected back (Fig. 1 *d*) until the edge of the levator ani muscles could be located and grasped on each side (Fig. 1 *e*). The levator ani muscles were sutured together in the midline with interrupted sutures of chromic catgut (Fig. 1 *f*). The submucous tissue was then united over the approximated muscles (Fig. 1 *g*). Finally, skin flaps were raised laterally and slid over across the newly constructed perineal body (Fig. 1 *h*).

The wound healed by first intention without any drainage. The patient was able to control her bowel movements perfectly without any soiling of the clothes. When she was dismissed from the hospital, the anus was separated from the vagina by  $1\frac{1}{2}$  inches (3.7 cm.) of skin, and a firm rectovaginal septum was present.

## COMMENT

A recent letter, which expressed the happiness of the parents and the patient with the result of the operation, further attests to the efficacy of the operative procedure.

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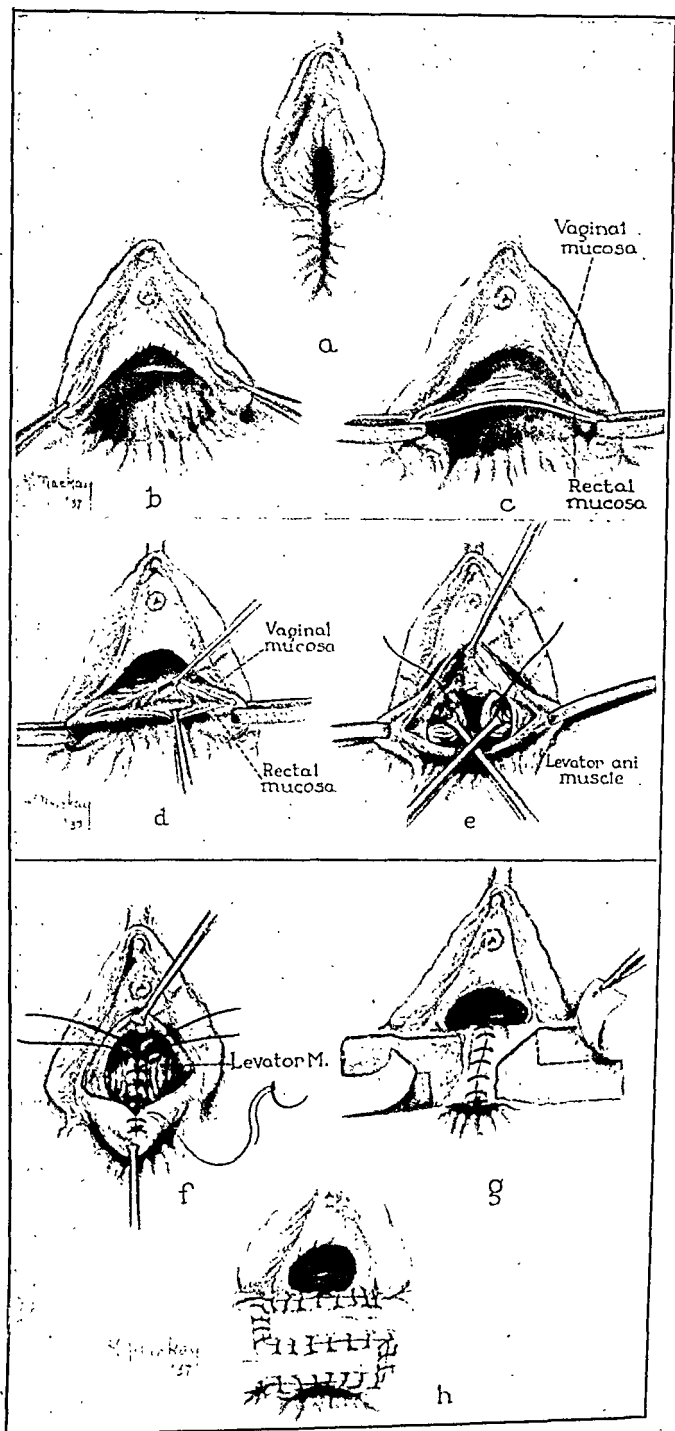


Fig. 1.—Repair of rectovaginal cloaca; *a*, condition of patient before operation; *b*, the labia are parted and upper part of incomplete rectovaginal septum can be seen; *c*, incomplete rectovaginal septum has been pulled down with tenaculum forceps and incision made in its free border; *d*, separation of the rectal and vaginal mucous membranes; *e*, dissection and isolation of the levator ani muscles; *f*, levator ani muscles are approximated in the midline; *g*, reconstruction of perineal body; *h*, use of skin flaps for plastic closure.

of the hospital and its bed capacity. Beginning in 1934, there was added considerable other information of assistance to prospective candidates, such as the percentage of free and pay patients, the percentage of autopsies, the number of residencies, and whether or not there was an out-patient service. Beginning with the issue of 1937, a further valuable addition was made in that the posts were divided into residencies and assistant residencies.

A study of the figures submitted in these publications has been made, utilizing certain criteria for inclusion of a residency as desirable for men wishing to qualify for the American Board of Surgery. The criteria utilized in the selection were 20 per cent or more free beds\* and an out-patient service. It was felt that if a hospital did not have at least this number of free beds, it could not possibly give to the young surgeon in his later years of training the *adequate operative experience in which the candidate had assumed the complete responsibility* as is demanded by the Board of Certification in Surgery. Utilizing these standards, we find the following number of approved residencies: 1934, 417; 1935, 439; 1936, 456; and 1937, 603. The figure for 1937 may be further divided into 248 residencies and 355 assistant residencies. These figures show a steady gain in the number of the posts available, but if one examines the figure critically it is noted that the great percentage of the posts offered are for one year only and there is no intimation given in the data that such a post may be continued a second year with increased responsibilities. Moreover, it is known that a very considerable number of these residencies are posts for which a man qualifies after a single year's previous training, training which, in fact, may be on a rotating service where the amount of surgical experience has been meager. It would be desirable if the Council on Medical Education and Hospitals could extend somewhat the amount of information given concerning the approved residencies and assistant residencies. Thus the addition of an item describing the amount of work the interne should have had before he can qualify for the post of assistant resident would be very helpful. There obviously is no comparison between the responsibility which can be given to a resident in surgery who has had a rotating internship and the responsibility which can be given to a resident surgeon who has had not only a one- or two-year straight surgical internship but in addition has had one or two years as assistant resident surgeon. There should be some way of bringing this information to the young surgeon. The splendid work accomplished by the Council of Medical Education and Hospitals in elevating the character and diminishing

\*I have interpreted "free" or "charity" beds as beds occupied by patients who are a direct responsibility of the hospital rather than of a private physician and thus might be utilized as a source of material for giving experience to properly qualified men under the guidance of responsible members of the hospital staff. "Private" as opposed to "charity" patients obviously cannot be used for this purpose.



# Editorials

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## Opportunities for Graduate Training in Surgery

THE American Board of Surgery has shouldered upon the surgeons of our country a great responsibility. The qualifications demanded for examination by the Board specify certain periods of training in hospitals and medical schools after receiving the degree of M.D.: (1) an internship of not less than one year, (2) further training in surgery in hospital and medical school of not less than three years, (3) adequate operative experiences in which the candidate has assumed the whole responsibility, and (4) an additional period of not less than two years of study or practice in surgery. The natural corollary to these demands is that there be places where a prospective candidate may secure this experience. Are there such places and are there a sufficient number of such places to educate all the men who should have and would like to have this experience?

After a personal survey of a large number of medical centers and hospitals and after a careful study of the very valuable data compiled each year by the American Medical Association and published in the hospital or educational numbers of their journal, I am convinced that the opportunities now afforded to fulfill the qualifications demanded by the American Board of Surgery are inadequate.

The material published for many years by the American Medical Association in the hospital number of the *Journal* is of considerable value to the young medical graduate in choosing the hospital to which he may go for further education. These tables, however, do not contain lists of posts beyond the internship, nor do they specify the percentage of free beds nor the autopsy percentage, which are prime criteria for the student to study if he is to choose a hospital where his experience will be considerable and instructive. In addition to the information in this number, the American Medical Association has published in their educational number for many years data concerning hospitals, at first listing hospitals approved for internships by the Council on Medical Education and Hospitals of the American Medical Association. In the last five years it has published a separate list of hospitals approved for residencies as well. The lists of such approved residencies in the educational number of the *Journal of the American Medical Association* are not of great value preceding 1934, because in the years antecedent to that time the list contained merely the location

of the patient, let alone this educational responsibility of the hospitals, there is every reason why adequate residencies should be established. The addition of such a person to a hospital staff leaves in the hospital at all times a man well equipped for surgical emergencies. It also leaves a mentor and leader for the house staff, someone who will see that the internes are taught the innumerable little things they should know about dressings and the care of the patient. Such an incumbent gives confidence to the patient and allows the trustees to feel that the hospital is adequately covered at times when the visiting staff are not at hand.

A great step forward was made when the American Board of Surgery set up such stringent qualifications. It now behooves all of us to make possible the postgraduate training of the young surgeon so that the qualifications demanded can be met and fulfilled.

—*Elliott C. Cutler, M.D.*

Boston, Mass.

### Is Judgment Necessarily Inarticulate?

THE beginner in medicine learns by a hard road certain elementary facts about the body and its abnormalities, facts chosen for their relationship to disease and the treatment of disease. When he first approaches the patient, he seeks to apply this knowledge to a particular clinical problem. At the outset his progress is slow and stumbling; his facts are incomplete and he has not yet learned their relative importance, nor the trick of combining them into a logical composite. As his experience with disease enlarges, these crudities diminish and, after a time, he becomes able to visualize the patient as a whole, the place of the presenting disease in the picture, and the rational treatment to be applied. When he has developed the ability so to apply facts tempered by experience that in a good proportion of instances the outcome of the case points to no mistakes in its handling, he is said to have developed judgment.

Essentially, judgment is a memory and association phenomenon, being developed more quickly the wider the professional reading and the more catholic the clinical contacts. The man who can most pertinently gather together scattered observations from his experience and make them refer to the individual case is the man most assured of exercising good judgment. But there is implied another factor, which we profess to recognize in the field of medical education; namely, the ability to express reasons for conclusions. If a doctor can say "I am proposing to carry out this treatment because . . ." and can clearly express the rationale of treatment, one is more impressed by his decision as embodying good judgment than if he is

the number of our medical schools by a system of grading suggests that a similar plan be adopted in regard to hospitals.

In adopting a system of rating or grading hospitals for graduate training in surgery, it would be necessary to grade or rate them on a descriptive plan, grouping separately (1) hospitals approved for undergraduate teaching, (2) hospitals approved for graduate training, and (3) hospitals of great community value whose clientele is mostly private. Such a plan would place no affront on the splendid private hospitals performing a most useful community purpose, as would occur if only teaching or training institutions were graded. Moreover, such a grading of all hospitals would serve another most useful service by stimulating boards of trustees to better their own institutions. Thus, a Grade "A" Hospital in each group would be representative of the best qualifications in that group. In the group fitted for the graduate training of the surgeon, Grade "A" would signify hospitals which had some tie-up with a medical school in order that the qualifications under the head "Special Training" in the booklet of information put out by the American Board of Surgery be fulfilled. Moreover, in this group a Grade "A" Hospital would have to have some set-up whereby it could train a young surgeon for at least three years following his first year of internship. Such restriction would unquestionably pull down the now 603 listed residencies and assistant residencies and would perhaps leave us in the Grade "A" group of those hospitals suitable for the graduate training of the surgeon a mere 10 per cent of the 603 residencies and assistant residencies listed in the 1937 educational number of the *Journal of the American Medical Association*.

If we consider that the country needs somewhere around 8,000 general surgeons, active, between the years of forty and sixty, and that in this group there is a 5 per cent mortality and a 5 per cent retirement rate yearly, then we need around 800 new surgeons each year. If all are to be qualified by the American Board of Surgery, it means that 800 suitable posts should be available each year in hospitals connected with medical schools. This does not mean that only hospitals in close physical relation with medical schools can be considered. It would be entirely feasible for those hospitals that are distant from a medical school to make some arrangements with a school whereby men at a certain point in their period of clinical training could receive more experience in the basic medical sciences in the medical school.

The task of increasing the number of posts where men can be adequately trained in surgery after graduation from medical school is the responsibility of each and every surgeon. We must all urge the establishment of further residencies in surgery and assist in every way to work out a liaison between medical schools and hospitals not now having such a connection. From the point of view of the care

who are not sensitive to the proper demands of the young assistant for instruction. It may not be presumptuous to suggest that in the daily contacts of hospital practice the surgeon make the attempt not only by precept but also, even more importantly, by example, to inculcate the idea that no essential mystery resides in the exercise of judgment, that implied or actual expression can be found of the reasons for any act of judgment, and that this hard way is the path toward the greatest reward in terms of further development.

—*Edwin P. Lehman, M.D.*

University, Va.

able to say only "I am proposing to carry out this treatment but I cannot tell you why." We insist on the student's writing down his opinion and the reasons therefor. It is recognized as good hospital practice to demand that the surgeon before operation commit himself to a diagnosis and give the reasons for operating.

In spite of this accepted relationship between clear thinking (implying good judgment) and clear expression, there remains in the philosophy of the profession a conception that may be regarded as an anomaly; namely, the idea of the existence of a somewhat mysterious gift, which descends upon a man after a number of years of experience, called "Judgment," a faculty so esoteric that the reasons for its conclusions cannot be expressed in words. It needs no profound research in medical literature, particularly that of presidential, commencement, and memorial addresses, to gain the impression that this faculty is the more revered the less articulate it is. This conception even creeps into the clinical literature. One may quote, for example, from a recent paper in this Journal: "It is just here that the surgeon of experience can tell that the patient is much sicker than he appears to be. He will not be able to state why he thinks so, if pressed by his colleagues."

There is no doubt, of course, that articulateness varies between men of equal judgment; in some men thought readily is transmuted into speech, whereas in others the transmutation is difficult. That fact does not negative the principle, however, that the clearer the thought the more easily it is expressed. One need not insist that every act of judgment be analyzed in the spoken or written word. It seems desirable, however, to make the point that inarticulateness is not an essential quality of good judgment. One may wonder if the contrary idea may not represent a vestigial psychologic remnant of the medical beard and frock coat, or even of the priesthood age of medicine, when mystery was of the essence of practice.

The matter is of most importance and interest in relation to the growth of the young medical mind. The contradiction between the teaching that clear thinking means clear speech, and the conclusion that the acme of medical attainment is necessarily associated with inarticulateness, must be obvious to the beginner. The young doctor cannot be much censured if this contradiction should lead him to conclude that the former teaching is not of great weight when the best of his siders can reach their most brilliant conclusions without being able to tell why. The temptation is presented to neglect the intermediate steps that demand the hard discipline of putting reasons into words, and to wait inertly, but more or less hopefully, for the golden moment when the great gift of Judgment will descend like a halo.

Although few hold formal teaching positions, there is no established surgeon of this present day who does not teach; and there are few

The method of Berkow,<sup>31, 32</sup> 1924, 1931, of estimating the surface area of various portions of the body in the study of burns is of great practical value, especially in any attempted statistical analysis of recovery percentage.

### SHOCK IN BURNS

I. *Relation to Shock From Other Types of Trauma.*—Another influence that has affected the study of burns is that gained from the study of traumatic shock in general. Burns are but a type of trauma, thermal in this instance, and trauma is but a noxious influence which, when severe, overtaxes the compensatory and recuperative powers of the animal organism. Much work has been done on the subject of traumatic shock in the past ten years. Previously the chief theories as to the origin of shock were the nervous and the toxic theories. In 1930 a physical theory was introduced and more recently the adrenal gland has been implicated.

Important general studies on the subject of shock have been published by Cannon,<sup>33</sup> 1923, in book form and in articles by Cattell,<sup>34, 35</sup> 1920-1923; Cannon and Cattell,<sup>36</sup> 1922; Erlanger and Gasser,<sup>37-39</sup> 1919; Erlanger, Gesell, and Gasser,<sup>40</sup> 1919; Porter,<sup>41</sup> 1919; Rukstinat,<sup>42</sup> 1932; Orr,<sup>43</sup> 1935; Frazier,<sup>44</sup> 1935; Coonse, Foisie, Robertson, and Aufranc,<sup>45</sup> 1935; Andrews,<sup>46</sup> 1935; Phemister,<sup>47</sup> 1935; Blalock,<sup>48</sup> 1930; Parsons and Phemister,<sup>49</sup> 1930; Mann,<sup>50, 51</sup> 1915-1918; Mann and Essex,<sup>52</sup> 1935; Seeley, Essex, and Mann,<sup>53</sup> 1936; Lambret and Driessens,<sup>54</sup> 1937; Moon,<sup>55-59</sup> 1934-1936; and most recently, Rein,<sup>60</sup> 1937. It is to be remembered, however, as pointed out by Simonart,<sup>61</sup> 1930, that the problem of shock in burns may be quite separate from that of shock due to other types of trauma.

### II. *Theories as to the Origin of Burn Shock.*—

A. *Nervous and Adrenaline Theory.*—A purely nervous theory of causation of shock and death in burns is not generally held. This is quite contrary to the case with traumatic shock in general where many workers support a purely nervous theory. In burns the immediate effect of the painful injury may be a syncope or primary type of shock, but usually by the time the physician sees the patient this is over. It is only later that secondary shock develops.

Consistent with the multiplicity of other theories of causation of shock in burns, several separate theories are attached to the adrenals alone. Both the medulla and cortex are indicted separately and besides several authors, arguing chiefly from necropsy evidence, have attributed death to the adrenals as a whole.

In this latter category Bardeen,<sup>62</sup> 1898, was one of the earliest experimenters. This author noted no pathologic changes in the adrenals in five necropsies. Weiskotten,<sup>63, 64</sup> 1917, 1919, on the other hand, found adrenal changes in ten necropsies following uncomplicated superficial

# Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

## RECENT ADVANCES IN THE STUDY OF BURNS

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### INTRODUCTION

THE study of burns has made rapid strides since the introduction of tannic acid by Davidson<sup>1-5</sup> from 1925 to 1927. These years may indeed be termed a turning point in the treatment of burns. Numerous variants of Davidson's original tanning technique have given rise to a multitude of new methods. Research and clinical observations have been made which support the tanning principle and, contrariwise, numerous opponents of this principle have put forth valid objections to it. Hence, at the end of ten years of use of the new treatments, somewhat of a perspective can be gained. They have, to a limited extent, been tested by time and it is appropriate to take stock of their efficacy.

Reviews of the treatment of burns before the tannic acid era are given by Sherman,<sup>6</sup> 1918, and by Ravdin and Ferguson,<sup>7</sup> 1925. More recent reviews are those of Seeger,<sup>8</sup> 1937; Baueroft,<sup>9</sup> 1937; Douglas,<sup>10</sup> 1934; Dunbar,<sup>11</sup> 1934; Barnes,<sup>11a</sup> 1933; Pack,<sup>12</sup> 1934; the book by Pack and Davis,<sup>13</sup> 1930; and the series of articles by Wilson,<sup>14-20</sup> 1928-37. Shorter reviews are those of Pack,<sup>21</sup> 1926; Snedecor,<sup>22</sup> 1935; and Pfohl,<sup>23</sup> 1936. Probably the best recent review of experimental work is that of Lambret and Driessens,<sup>24</sup> 1937. The most recent clinical review is that of Fasal,<sup>25</sup> 1937. Pack,<sup>26</sup> 1926, gives a discussion of the medicolegal aspects of burns and scalds. Fasal,<sup>27</sup> 1937, gives a discussion of the various causes of burns.

The number of deaths from burns during the last few years has averaged about 6,000 per annum in the United States. This about one-sixth the number dying from automobile accidents. However, since the latter represent a myriad of types of injury, the importance of study of burns becomes more manifest as with them, if treatment is efficacious, benefits may be obtained. The death rate from burns is improving of late<sup>28</sup> especially in younger children.<sup>29</sup> Riehl,<sup>30</sup> 1933, reports a very severe burn in a newborn infant with temporary recovery which he attributes to transmitted resistance.

and kidneys as well as other organs causing fatty degeneration. He also reported the blood of burned rabbits was toxic when injected into other animals. In an extensive monograph Pfeiffer,<sup>86</sup> 1905, in experiments on guinea pigs and rabbits reported that deaths in the first two to six hours are due to shock, while thereafter they are caused by decomposition products of burned protein which he reported he isolated.

Robertson and Boyd,<sup>87, 88</sup> 1923, reported very definite results in their search for a burn toxin. After producing skin, subcutaneous tissue, and muscle burns experimentally, they reported finding a burn toxin that was present in whole blood and cells, but not in the serum. Therefore it was absorbed on the cells. They reported that alcoholic extracts of burned skin would produce symptoms when injected intraperitoneally or intravenously into experimental animals, but that these results did not follow the injection of similar extracts of normal skin or skin of animals burned after death. They reported that blood from burned animals injected into guinea pigs produced toxic symptoms and "autopsy findings in the fatal cases were identical with those seen in burned animals." They claimed to have separated a thermostable neurotoxic and a thermolabile necrotoxic element in their toxin, which toxin consisted of primary and secondary proteoses. Because of the presence of this toxin, they advised exsanguination transfusion and concluded: "From a purely clinical point of view, there seems to be no doubt that the burned tissues are responsible for the production of some toxin which is taken up by the blood stream."

Underhill and Kapsinow,<sup>89</sup> 1931, repeated the work of Robertson and Boyd on the injection of alcoholic extracts of burned skin and reported that the control extracts were fully as lethal as the extracts of burned skin and the lethal factor in either case was merely the alcohol. They correlated the irregular action of the control extracts with the lack of a statement in Robertson and Boyd's papers on the number of controls done. Underhill and Kapsinow concluded: "Our experience with burns leads us to doubt the existence of a 'burn toxin,' and to believe that the persistence of this viewpoint is an obstruction in the way of clarification of the burn problem."

Underhill, Kapsinow, and Fisk,<sup>90</sup> 1930, presented data which showed delayed absorption of such substances as strychnine and phenolsulphonaphthalein from burned areas. Since there was fluid loss from the capillaries, they thought that these absorption experiments showed that the increased permeability was in one direction only, namely, from the blood into the tissues. Mason, Paxton, and Shoemaker,<sup>91</sup> 1936, performed experiments somewhat similar to the preceding ones, only they used a substance of low molecular weight for their absorption tests, sodium iodide. This was excreted in almost identical quantities in the urine of burned and control animals after subcutaneous injection, the



burns. Greenwald and Eliasberg,<sup>65</sup> 1926, and Berkow,<sup>66</sup> 1931, also found adrenal changes. Inouye,<sup>67</sup> 1933, and Lattes;<sup>68</sup> Salvioli;<sup>69</sup> Hartman, Rose, and Schmidt;<sup>70</sup> and Olbrycht<sup>71</sup> also reported work inculcating the adrenals. Brooks and Blalock,<sup>72</sup> 1934, however, present evidence to show that somewhat similar adrenal changes will follow hemorrhage and trauma to muscles, indicating that they are not specific to burns.

Freeman,<sup>73</sup> 1935, and Freeman, Shaw, and Snyder,<sup>74</sup> 1936, and Freeman,<sup>75</sup> 1937, have proposed a theory of shock that consists in essentially an overexcretion of adrenalin to keep the blood pressure near normal despite a lowered blood volume. If the blood volume decreases more, and this it tends to do because of capillary exudation with increased arteriolar resistance, the increased adrenal output can keep the blood pressure compensated only so long and then it collapses. Thus, this theory proposes that an overproduction of adrenalin is a factor. Saito,<sup>76</sup> 1932, believes, contrariwise, that in burns a deficiency of adrenalin is the chief factor and he has prolonged the lives of experimentally burned animals by intraperitoneal adrenaline injections (average length of life of injected burned animals sixty-three hours; of control burned animals, twenty-seven hours). Riehl,<sup>77</sup> 1928, on the other hand, does not believe that adrenalin is a factor.

Other writers have accused the cortex as being the site of injury with resultant hypofunction and death. Swingle, Pfiffner, Vars, Bott, and Parkins,<sup>78</sup> 1933; Swingle and Parkins,<sup>79</sup> 1935; and Donahue and Parkins,<sup>80</sup> 1935, reported experiments tending to show a similarity between adrenal cortical insufficiency and traumatic shock. The injection of "cortin" was said to control the insufficiency and combat the shock. This work was immediately supported by Heuer and Andrus,<sup>81</sup> 1934, and attacked by Freeman,<sup>82</sup> 1933, and Britton and Silvette,<sup>83</sup> 1933, amidst extensive polemics. Wilson, Rowley, and Gray,<sup>84</sup> 1936, have taken the practical application of extract of suprarenal cortex from this discussion. They used this extract in three cases of burns, two of which they believed would have died otherwise. However, they mention that no sweeping conclusions can be drawn from this small series.

*B. Toxic Theory.*—From the very start of interest in burns, the toxic theory has been in the forefront as an explanation for the cause of shock and resultant death. Scores of poisons have been indicted, most often on an entirely empirical or theoretical basis, and the very number of suspected toxic substances is one of the chief evidences against positive proof for a toxic basis. On the other hand, just because some of the recent work has been against a toxic theory for death in other kinds of shock, this has no absolute bearing on the subject of burns, for they represent a separate problem.

Parascandolo,<sup>85</sup> 1904, was one of the early experimental proponents of the toxic theory. In work on rabbits he reported that death was due to toxic poisoning caused by a circulating substance acting on the liver

in four animals where it was observed one hour after burning and that these latter animals recovered. The other animals, four of which died under three hours and the remaining four dying from ten to sixty hours after the burn, showed hemolysis only in the fifteen-minute sample. Furthermore, the hemolysis stopped while the blood was still concentrating, all of which tends to prevent one from accepting Ishizawa's postulates. Murai,<sup>99</sup> 1933, has studied the effects of injections of heated skin and gastric mucous membrane extracts, finding the former more toxic. Ravdin and Ferguson,<sup>7</sup> 1925, and Davidson,<sup>1-5</sup> 1925, 1927, favored the toxic theory. Davidson's whole tannic acid therapy was founded on the concept of prevention of toxin production by an absorption from injured or autolyzed tissue and was instituted at the suggestion of Mason.<sup>91</sup>

Harkins, Wilson, and Stewart,<sup>100</sup> 1935, presented work that was evidence against the toxic theory. They made protein-free extracts of normal and burned skin of rabbits by means of trichloroacetic acid extraction. The extracts of normal skin contained a depressor substance which was not acetylcholine, adenosine, histamine, or the "P" substance of Euler and Gaddum,<sup>101</sup> 1931. Extracts of rabbits' skin, to which heat had been briefly applied at intervals of from three minutes to 48 hours previously, contained an apparently identical depressor substance. Such extracts showed no increased depressor activity, but sometimes a diminution, which is probably due to dilution of the depressor content of normal skin by edema fluid. Later, Wilson, Jeffrey, Roxburgh, and Stewart,<sup>20</sup> 1937, again used rabbits as the experimental animal, but this time they did not use protein-free extracts and this time the extracts did show evidence of toxic action. The edema fluid which accumulated in the burned area gradually acquired toxic properties and, when collected forty-eight hours after burning, it was frequently lethal to healthy animals of the same species. The development of toxicity was independent of the action of bacteria and seemed to be related to the autolysis of injured tissue. The toxic principles were associated mainly with the globulin fraction and their action was on the nervous and circulatory systems and in the production of degeneration of liver cells. This work is further discussed by Roxburgh,<sup>102</sup> 1936, and in an editorial in the *British Medical Journal*,<sup>103</sup> 1937.

Cattrano,<sup>104\*</sup> Boyer,<sup>105</sup> Guinard,<sup>106</sup> Vegt and Vaccarezza,<sup>107</sup> Kozareff,<sup>108</sup> and Massabuau, Laux, and Ginestíé,<sup>109</sup> 1935, favor the toxic theory. Bernhard,<sup>110</sup> 1936, found that extracts of experimentally burned skin were toxic when injected into other animals. From autopsy changes in the case of a girl aged four years dying seventeen days after a third degree scald of the left hand 9 by 5 cm. in area, with the observation of changes in the heart muscle and kidneys, Brenner,<sup>111</sup> 1936, favored the toxic theory. The size of this burn and death after the time when infec-

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injection being made in the case of the burned animals into the skin of the burned area on the abdomen six hours after burning.

Harrison and Blalock,<sup>92</sup> 1932, performed experiments, the results of which opposed the toxic theory. These were repetitions of experiments that had been reported by others as favoring the toxic theory. (1) The transplantation of burned skin had no effect on the recipient animal. (2) The effects of débridement on the survival period of burned dogs: the survival averaged seven and one-half hours in the débrided series and seventeen and one-half hours in the control dogs. (3) Transfusion of blood from burned to normal animals was without effect. Blalock and his associates,<sup>133-135</sup> 1931, reported work favoring the loss of plasma-like fluid being a potent cause of death following burns (see section of physical theory), but Mason and others,<sup>91</sup> 1936, quote him as saying in 1934: "I believe that deaths which occur from three to ten days following severe burns are due in large part to the absorption of protein decomposition products." Straus,<sup>93</sup> 1937, working in Karsner's laboratory, was unable to isolate substances in burned guinea pigs which, when injected into other animals, would act like a toxin.

Japanese investigators, on the other hand, have practically invariably supported the toxic theory. Nagamitsu,<sup>94, 95</sup> 1933, 1935, found that blood serum or fluid perfused through the burned hind limbs of dogs or rabbits when tested on cat's blood pressure or guinea pig's uterus or intestine showed a histamine-like depressor action. However, the action was not abolished by histaminase. Shimada,<sup>96</sup> 1934, believed that the burn toxin is nothing other than histotoxin which can be differentiated from histamine by its action on the toad's kidney. Miura,<sup>97</sup> 1934, perfused the burned hind legs of rabbits and found a toxin. Inouye,<sup>67</sup> 1933, has seen autopsies of three burned patients with changes in the adrenals. He believed the changes in burns are much the same as those caused by strychnine, barium chloride, and picrotoxin. He said that Pfeiffer,<sup>98</sup> 1905, attributed these changes in the adrenals (disappearance of lipid bodies, loss of chromaffine affinity, hemorrhage, hyperemia, and focal necrosis) to the accompanying low blood pressure due to shock. He further quoted Kolisko, Nakata, and Niemeyer as postulating that a toxic action caused the adrenal changes and that the adrenal injury in turn killed the animal. On the other hand, Takeuchi said that the adrenal changes are only a part of the general picture and not the direct cause of death. Inouye, himself, adhered to Takeuchi's theory but believed also that the adrenal damage may be one of the factors in the causation of death. Ishizawa,<sup>98</sup> 1935, from experiments on rabbits, postulated that the hemolysis of red cells at the site of the burn gives rise to a toxic substance and is the cause of early death in burns. A hemoglobin discoloration of the plasma was often found as early as fifteen minutes after a burn. A study of this paper reveals that such a hemoglobin discoloration of the plasma was only observed at fifteen minutes except

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said to rest upon adequate experimental work at present." Simonart,<sup>61</sup> 1930, also found no evidence for a toxic action. Lesser,<sup>115</sup> 1880, attributed the toxic action of burns to a functional impairment of the red cells that pass through the burned area making them foreign to the organism and giving rise to anemia in the functional sense.

A session of the 1937 French Surgical Congress (held in Paris in October) was devoted to the subject of burns.<sup>116</sup> Pierre Duval (cited also by Rudler,<sup>117</sup> 1935) gave a report favorable to the toxic theory. He believes that autolyzing tissue at the site of the burn acts as a toxin. He reported that in animals it was found that repeated burns conferred a state of sensitization, which in turn confers a certain immunity or resistance toward burns. Mourge-Molines advocated silver nitrate-tannic acid treatment to combat the toxemia and in the discussion McClure, of Detroit, spoke in behalf of tannic acid. Riehl, of Vienna, advocated blood transfusion, tannic acid, and, in many cases, saline baths. Wilson, of Edinburgh, advocated 20 per cent tannic acid, gentian violet, and acriflavine to combat infection and adrenal extracts to combat toxemia. Seemen, of Munich, advised electrocoagulation of the burned surfaces. Donati, of Milan, endorsed the methods which aimed to prevent dehydration and intoxication. Leriche, of Strasbourg, found that tannic acid treatment did not prevent humoral changes, and he uses mercurochrome in children and in infected burns. After the first few days of a burn, Piollet and Limousin, of Clermont-Ferrand, use cod liver oil dressings. The keynote of the entire meeting was in harmony with the toxic theory. Rudler,<sup>117</sup> 1935, was one of the first to use tannic acid in France.

The experiments of Rosenthal,<sup>118, 119</sup> 1937, are one of the most recent units in the evidence for the toxic theory. If these can be confirmed, they certainly represent strong reasons for adopting this idea. Rosenthal found a substance that caused contraction of the virgin guinea pig uterus in the blood of burned shoats, adult pigs [sic], guinea pigs, and human beings. This substance was at first linked with the red blood corpuscles, but it was later found in the serum. It differed from histamine in several ways. The sera of shoats, pigs, and human beings that were burned were tested in the healing stage and found to neutralize histamine and "burn toxin" as tested on the guinea pig uterus. However, normal serum has this action to some extent. No controls using blood concentrated by some other means than by burning alone were used in these experiments.

*C. Bacterial Theory.*—Aldrich,<sup>120</sup> 1933, at the suggestion of Firor, aroused interest in this theory and to combat bacterial action gentian violet was introduced as a method of treatment. For the first twelve hours, the burn areas were found to be sterile. After this period, it was found that in 100 per cent of the severely burned patients and in a large majority of the minor burns the beta-hemolytic or gamma strep-

tion had taken place might indicate that death in Brenner's case was due to infection rather than autolytic toxins. It is to be pointed out that one definition of a burn is "an infected wound produced by heat." Catiano,<sup>112</sup> 1882, believed that when ammonium formate, derived from the sweat, was heated in the process of burning skin, it lost water and became HCN, the cause of the toxic action of burns.

Barsoum and Gaddum,<sup>113</sup> 1936, reported a rise in blood histamine in burned patients reaching a peak of five times normal seven days after the burn. They stated, however: "The relation of this rise in blood histamine to secondary shock is uncertain. There was no clear evidence of any correlation between the blood histamine and the clinical condition of the patient." The rise was possibly due to interference with the function of the kidneys or other histamine-excreting mechanisms. The rise occurred later than the time of secondary shock, but the writers attributed this to the fact that the patients were Egyptian!

Fender,<sup>114</sup> 1933, gave an excellent review of much of the earlier work favoring the toxic theory, listed seventeen toxins proposed by thirty-four different workers, and showed that many of their experiments are open to question (see Table I). Merely because there is confusion as to the name of the toxin is of course not evidence against its presence. Fender found changes in the spleen and lymph glands of burned rabbits, but he concluded: "The theory of causation of death by a toxin cannot be

TABLE I  
PARTIAL LIST OF TOXINS POSTULATED AS THE CAUSE OF BURNS\*

NO.	TOXIN	AUTHOR
1.	Ammonia	Edenhuizen
2.	Ammonia or urea	Billroth
3.	Fibrin ferment	Foa
4.	Urea	Ponfick
5.	Hydrocyanic acid	Catiano <sup>112</sup>
6.	Ptomaine	Lustgarten, Kitjanitzin, Parascandolo <sup>85</sup>
7.	Pyridine base	Reiss
8.	Hemolysins and hemoagglutinins	Von Dieterichs
9.	Choline-like substance	Kohlrausch
10.	Methyl guanidine	Heyde
11.	Diamino acids	Eden and Herimann
12.	Primary and secondary proteoses	Robertson and Boyd <sup>87, 88</sup>
13.	Peptone	Olbrycht
14.	Inorganic intracellular material	Turck
15.	Unspecified protein cleavage products	Pfeiffer, <sup>86</sup> Fraenkel and Spiegler, Brancati, Il Seung O, Nishimura Ardakoff, Boyer and Guinard, McCrae, Scholz, Vacarezza, Bardeen, <sup>62</sup> Weiskotten, <sup>63, 64</sup> Pack, Davidson, <sup>1-5</sup> Speese and Bothe, Weidenfeld
16.	Unspecified toxin	Schjerning Dorrance and Bransfield Tuder
17.	Potassium salts	Stengel and Fox
18.	Toxalbumin	
19.	Anaphylaxis	
20.	Abrin and ricin-like toxin	

\*Adapted from Fender,<sup>114</sup> 1933, and Pack,<sup>21</sup> 1926.

during the first twenty-four to forty-eight hours, which is the time when shock with blood concentration and low blood pressure, low cardiac output, and low blood volume occur. Death from true secondary shock usually occurs in the first day after the burn, which is earlier than infection becomes active.

D. *Fluid Loss (Physical) Theory*.—Underhill and his associates,<sup>125-132</sup> 1923-1930, were the first to draw attention to the extensive local loss of fluid in burns. Previously (*vide infra*) the blood concentration resulting from such fluid loss had been noted. Underhill and his associates produced experimental burns and found that the edema at the site of the burn reached a maximum at the end of twenty-four hours and was reabsorbed in five to six days. Chemical analysis of this edema fluid showed it to be closely similar to blood plasma. Underhill measured the amount of this edema fluid by squeezing it out of the soggy tissues and found it to be equal in some instances to 70 per cent of the total blood volume.<sup>131</sup> Loss of such fluid is of much more serious consequence than loss of an equal amount of mere watery transudate. As the writer has pointed out, a person can urinate three liters a day, but can hardly part with a similar volume of blood in the same time.

Blalock,<sup>133</sup> 1931, determined the amount of fluid lost into the tissues by burning one side of the animal and then bisecting the animal and comparing the weight of the two sides. In a series of burned dogs the edema fluid averaged 3.34 per cent of the body weight (about one-half of the plasma volume). In plasmapheresis experiments Blalock found that 3.5 per cent of the body weight of plasma removed would kill the animals. The edema fluid in Blalock's experiments was similar to plasma as shown by Beard and Blalock,<sup>134</sup> 1931, and hence in the burned animals enough plasma was lost to kill them alone without invoking the action of any toxin at all, although the author makes no such sweeping conclusion. Johnson and Blalock,<sup>135</sup> 1931, next showed that the cardiac output was markedly decreased following burns.

The author,<sup>136, 137</sup> 1934-1935, performed experiments confirming Blalock's data when unilaterally burned animals were bisected. Furthermore he placed the burned animals on a tipping apparatus so that as the burned side grew heavier a kymographic tracing measured the weight shift. This furnished a graphic method of recording the local accumulation of fluid in experimental burns. The accumulation began at the time of the burn and continued in the form of a decelerating curve until death. Accompanying the collection of fluid was a simultaneous increase in the percentage of hemoglobin and in the hematocrit readings. After most of the fluid had accumulated, the fall in blood pressure set in and continued rapidly until death occurred in a state of secondary shock. The author,<sup>138, 139</sup> 1934, 1935, also showed that the bleeding volume of burned animals is markedly decreased. It is interesting in this connection that histamine does not appreciably lower the bleeding volume



tococcus could be grown from repeated cultures. The concentration of these organisms increased with the obvious signs of sepsis and the beginning of the toxicity of the patient, until after forty-eight to fifty-six hours pure cultures of the streptococcus could be obtained, having outgrown all the other organisms. Coincidentally, the characteristic bad effects of the burn were shown by the patient.

Clark and Cruickshank,<sup>121</sup> 1935, believed that infection of burns, particularly by *Streptococcus hemolyticus*, is common even with tannic acid and is responsible for the fever and toxemia during the first four or five days of the illness. Therefore, they added 20 per cent dettol to the tannic acid and even suggested the administration of scarlet fever antiserum. Cruickshank,<sup>122</sup> 1935, reported detailed bacteriologic studies of burns. He believed that the high incidence of infection by this organism is probably favored by the congregation of patients in wards, as he discovered hemolytic streptococci in the throats of patients more frequently during their first week in the hospital than at the time of their admission; these bacteria were numerous in the atmosphere and dust of the wards in which the burns were treated.

Marsh,<sup>123</sup> 1935, was an earnest and quite radical supporter of the bacterial theory, and, without showing in his paper that burns are affected by staphylococcal infection, went on to advise empirically that "every case of severe burn should receive intravenously at the earliest possible moment, an injection of staphylococcal antitoxin amounting, for an adult of normal size, to at least 5000 international units. . . . People constantly exposed to the risk of severe burns, by nature of their employment, could be treated prophylactically with a course of staphylococcal toxoid injections."

The writer,<sup>124</sup> 1936, reported that in a series of burns the only two fatal cases within the first three weeks resulted from sepsis. The first of these was a male, aged forty-four years, with second degree burns of the left leg, face, neck, thorax, and arms; third degree burns of hands and forearms, following a gasoline explosion. Blood concentration with hemoglobin, 140 per cent, and red count, 7,200,000, was noted twenty-four hours later. On the seventh day pyarthrosis of the left knee due to *Streptococcus hemolyticus* with a fever of 106.6° F. and death were noted. The second case, a child of four years of age, died eleven days after a second and third degree scald of the thighs, legs, buttocks, arms, one-half of the back, and almost the entire trunk anteriorly. The patient developed a peritonsillar abscess and thrombosis of the veins of the right arm with a fever over 104° F. each of the last six days of life and at necropsy a typical Curling's ulcer was found. These cases demonstrate that not only many of the toxic manifestations present after the first few days but also some of the complications of burns may be explained on the basis of a septicemia, although this is not conclusively proved. However, these cases do not have marked infection

these men might well be applied to burns to prevent possible harm to patients before the treatment of burn shock by injection of crystalloidal solutions is finally accepted. Certainly, until the matter is finally settled, if blood is available, blood should be given. Furthermore, even though the recipient's blood is concentrated already, the donor's blood is relatively dilute by comparison, so that the often cited objection to blood transfusion in the presence of blood concentration is not entirely valid. The use of saline and other crystalloid solutions should be undertaken with the full understanding that they may not only run right through the injured capillary walls but may carry valuable blood constituents with them, leaving the blood more concentrated in red cells and lower in plasma-volume than before. Working under other ideas, Gunn and Hillsman,<sup>145</sup> 1935, advise giving 5,000 c.c. of saline solution intravenously immediately in severe burns.

#### LOCAL TREATMENT OF BURNS

I. *Tannic acid*.—Chief credit for the introduction of tannic acid as a generally used therapy of burns should go to Davidson,<sup>1-5</sup> 1925-1927. Previous to this time tea had been used empirically by the Chinese (5,000 B.C.) and in the form of ink by the Jews and Filipinos. The older inks often contained more tannic and gallic acids than do the modern inks. McClure and Allen,<sup>156</sup> 1935, quote an article in the *Pittsburgh Medical Review*<sup>157</sup> of 1890 on the use of 5 per cent solution of tannic acid in burns.

The tannic acid treatment has been used extensively in this country by Fantus,<sup>158</sup> 1934; Penberthy,<sup>159, 160</sup> 1934-1935; Christopher,<sup>161</sup> 1930; Mason,<sup>162</sup> 1933; Bancroft and Rogers,<sup>163, 164</sup> 1926-1928; Beck and Powers,<sup>165</sup> 1926; Beekman,<sup>166, 167</sup> 1928-1929; Glover,<sup>168</sup> 1932; Walsh,<sup>169</sup> 1935; Seeger,<sup>170, 171</sup> 1932; Mc Elroy,<sup>172</sup> 1936; Wolfer,<sup>173</sup> 1936; Harkins,<sup>124</sup> 1936; Stanley-Brown,<sup>175</sup> 1935; and others. It has been used considerably in most of the European countries except France where Rudler,<sup>117</sup> 1935, is one of its supporters. Salzer,<sup>176</sup> 1928, of Vienna, reports good results following its use, while in Great Britain the treatment has been used especially by Wilson,<sup>14-20</sup> 1928-1937, and Mitchiner,<sup>146</sup> 1933.

Several aspects of the tannic acid treatment have been somewhat modified by recent reports. Seeger,<sup>170</sup> 1932, has shown the advisability of buffering the tannic acid solutions with sodium carbonate. Hartman and Schelling<sup>174</sup> also have studied the effect of pH on tannic acid. As done by Fantus at the Cook County Hospital in Chicago, buffering consists in using 7.95 gm. of anhydrous sodium carbonate to each 50 gm. of tannic acid that is used in preparing a 5 per cent solution. The use of a spray to apply the tannic acid instead of compresses as originally used by Davidson is now common practice except in the vicinity of the eyes. Various antiseptics have been added to the tannic acid to make it more bactericidal. Most authors believe that once pus has formed beneath

under similar experimental conditions when it has lowered the blood pressure to a shock level. Schievers,<sup>140</sup> 1936, has shown that the blood volume is reduced by as much as 50 per cent in experimental burns. He attributed this partly to destruction of red cells but mainly to transudation of plasma. This work fits in with that of the writer on bleeding volume and along with that of Simonart,<sup>141</sup> 1928, is one of the bases for Schievers' support of the physical theory.

Lambret, Driessens, and Cornillot,<sup>142, 143</sup> 1937, and Lambret and Driessens,<sup>54</sup> 1937, also have shown that there is a marked blood concentration and blood volume decrease in experimental burns. These authors base their treatment of burn shock on replenishing the lost plasma.

Mc Iver,<sup>144</sup> 1933, presented some evidence that may be taken to support the physical theory. He showed that in human patients the blister fluid was similar to blood plasma and that the hemoglobin and hematocrit readings were markedly increased in such patients.

Gunn and Hillsman,<sup>145</sup> 1935, give credit to several theories in a graphic sequential representation of events following a burn. Mitchiner,<sup>146</sup> 1933, also gives some credence to the fluid theory.

Weiner, Rowlette, and Elman,<sup>147</sup> 1936, reported marked blood concentration with most red counts above six million, two being over eight million in forty burned patients. They pointed out that the low plasma protein, due in this instance to plasma loss, is quite different from that in dehydration from diarrhea or vomiting where the plasma protein is elevated, being in some instances over 10 gm. per 100 c.c. In this connection McClure,<sup>148</sup> 1936, pointed out that very little of the fluid lost in burns is due to evaporation, the slight increase being due to increased surface temperature.

III. *Treatment of Shock.*—The treatment of burn shock advocated by most workers is similar to that used to combat other types of shock. Fluids, warmth, stimulants, and sedatives are advised. Blood transfusion is especially advocated as by Riehl,<sup>149, 150</sup> 1932, 1933. Since the blood is concentrated in burns, the possibility of giving intravenous plasma rather than whole blood is to be considered. This procedure is not generally adopted, but it is used by Lambret and Driessens,<sup>54</sup> 1937, and by Weiner, Rowlette and Elman,<sup>147</sup> 1936. Wilson,<sup>17</sup> 1935, has used gum acacia.

Several writers have reported that large quantities of intravenous saline or Ringer's solution alone may be harmful in cases of traumatic shock. Davis,<sup>151</sup> 1937, reported such a finding in experimental animals. Beard and Blalock,<sup>152</sup> 1932, reported this to be true in intestinal trauma. If a crystalloid solution is injected, it carries more protein out of the blood stream than would have been lost were the animal left strictly alone. Blalock, Beard, and Thuss,<sup>153</sup> 1932; Beard, Wilson, Weinstein, and Blalock,<sup>154</sup> 1932; and Blalock and Beard,<sup>155</sup> 1932, have reported a similar finding in other types of traumatic shock. The observations of

per cent and in another four-year period from 1924 to 1928 the mortality dropped to 6.6 per cent even though tannic acid was not yet introduced.

Most of the recently devised methods of burn therapy have been offshoots of the tannic acid precipitant method. Aside from the use of buffers mentioned above, considerable discussion has centered around the strength of solution to be used. Davidson originally introduced a 2.5 per cent solution; later most American clinics used 5 per cent, while in England, Wilson,<sup>19</sup> 1936, advocated a 20 per cent solution. Others have used various antiseptics with the tannic acid solution. Mitchiner,<sup>180</sup> 1933, advocated the use of 1-2000 mercuric chloride to make up the tannic acid solution. Wilson,<sup>17</sup> 1935, used 1-100 acriflavine and Clark and Cruickshank,<sup>121</sup> 1935, used 20 per cent dettol. Hartman and Schelling,<sup>174</sup> 1935, have studied the use of amyl trieresol in combination with tannic acid in vitro.

At the present time, as brought out in the discussion of Penberthy's recent article,<sup>181</sup> tannic acid spray is used at the Children's Hospital in Boston, tannic acid compresses at the Presbyterian Hospital in New York, and tannic acid baths at the Massachusetts General Hospital. Gentian violet is used at the Johns Hopkins Hospital and the New Haven Hospital. To these data it is to be added that tannic acid is used in St. Lukes Hospital, Chicago; Henry Ford Hospital, Detroit; Children's Hospital, Detroit; and in conjunction with silver nitrate at Children's Memorial Hospital, Chicago.

II. *Tannic Acid and Silver Nitrate*.—This modification of the tannic acid method was introduced by Bettman,<sup>183</sup> 1935, with the idea of hastening the tanning process. After application of 5 per cent tannic acid solution, "the entire area is sponged over with a 10 per cent solution of silver nitrate. The burned tissues become black almost immediately. All oozing and leaky areas are sealed at once and the patient is encased in an impervious antiseptic dressing that has formed in seconds instead of hours." Bettman reported on the further use of his method<sup>184</sup> in 1937; and it was adapted in New Zealand by Cotter and Kimbell,<sup>185</sup> 1935, and in England by Mitchiner,<sup>186</sup> 1936. In Sweden Kissmeyer,<sup>187</sup> 1936, used it in the form of an ointment on burns that are not severe enough to enter the hospital:

Rx	Ag NO <sub>3</sub>	0.25
	H <sub>2</sub> O	25.00
	Olive oil	25.00
	Wool fat	50.00

In a recent report Glover,<sup>182</sup> 1937, adapted the combined treatment instead of tannic acid alone such as he previously used.<sup>168</sup> With the silver nitrate, he now uses 10 per cent tannic acid. He states that with this combination coagulation is usually produced within thirty minutes and

the tannic eschar it should be evacuated and the elevated eschar cut away. Martinez,<sup>177</sup> 1933, of Liverpool, stands alone in adhering to the theory of laudable pus and advising that the crusts with infection beneath not be removed.

Taylor,<sup>178, 179</sup> 1936, brought up an important objection to the use of tannic acid. This author showed by microscopic sections that in many cases of so-called third degree burns there are remnants of viable deep-lying hair follicles and sebaceous glands. These cells may provide a focus for new growth of healthy skin. Taylor further showed that these very cells may be killed by the tanning process and advised that the treatment be used only in cases of life and death. This is only one of the objections to tannic acid, others being that its eschar is stiff and either prevents motion around joints or, if allowing it, cracks; that it is not bactericidal to any great degree (see section below on gentian violet); that it may delay skin grafting (see section below on saline soaks); that it cannot be used around the eyes; and that its rigid eschar may cut off the circulation to the fingers, etc.

Despite these objections, it has a wide use in reducing the mortality of severe burns, whether it does this by reducing the loss of plasma or by preventing the absorption of toxic products. Table II (enlarged

TABLE II

REPORTED REDUCTION IN MORTALITY FOLLOWING INTRODUCTION OF TANNIC ACID THERAPY OF BURNS

AUTHOR	OTHER METHODS		TANNIC ACID	
	NUMBER OF PATIENTS	MORTALITY %	NUMBER OF PATIENTS	MORTALITY %
Bancroft and Rogers (N. Y.)	90	40.0	114	20.0
Beekman (N. Y.)	320	37.8	114	14.9
Wilson (Edinburgh)	300	38.7	117	11.1
Mason (Philadelphia)	91	28.5	87	13.3
Harris (Toronto)	-	26.6	-	12.0
Langer (Vienna)	86	16.3	65	7.7
Mitchiner (London)	243	9.4	249	2.4
McClure and Allen (Detroit)	118	9.3	358	11.7
Glover (Cleveland)	121	14.0	556	10.2
Hempel-Jorgensen	-	40.0	-	11.0

from Glover,<sup>182</sup> 1937) shows the reduction of mortality effected by the introduction of tannic acid in several clinics. It is to be remembered, however, that burns differ in degree and that with improving public health standards more smaller burns may be hospitalized than formerly. Also, the general hygienic care and the treatment of shock with blood transfusion, saline infusions, etc., may be more adequate than formerly. McClure and Allen,<sup>156</sup> 1935, reported no decrease in mortality. Mitchiner,<sup>146</sup> 1933, reported that the mortality may decrease from other reasons than tannic acid treatment, such as better hygienic care. He stated that in the London Hospital the mortality from 1899 to 1903 was 25.3

have the added advantage of being antiseptic in their action. These methods will be listed separately below.

1. *Gentian Violet (Methyl Rosaniline)*.—This method was introduced by Aldrich,<sup>120</sup> 1933, at the suggestion of Firor. A 1 per cent solution is used as a spray in a manner identical to tannic acid. The method has since been used by De Hart,<sup>197</sup> 1936, and others. An objection to the gentian violet is that it discolors everything with which it comes in contact. Churchman and Herz,<sup>198</sup> 1913, showed that gentian violet was not very toxic. Certain rabbits were well, despite the fact that gentian violet in a concentration of 1-2500 was circulating in their blood stream. The dye disappeared from the blood promptly and stained the mucous membranes among other tissues.

2. *Brilliant Green*.—Koritkin-Nowikow,<sup>199, 200</sup> 1934, 1936, treated a series of 215 patients with a 1 per cent solution of brilliant green, 139 of which were second degree burns and 76 third degree. Of these nine, or 4.02 per cent, died.

3. *Brilliant Green Plus Acriviolet*.—Aldrich,<sup>201</sup> 1937, reports that this combination is preferable to gentian violet. He states that gentian violet is active in combating gram-positive organisms, e.g., *Streptococcus hemolyticus*, but that it is ineffective against the gram-negative organisms. The acriviolet used in the present method is a loose chemical combination between acriflavine and crystal violet and the new treatment provides the strongest antiseptic against the gram-positive organisms that will not injure living tissues and also has a high specificity against the gram-negative organisms. In broth cultures it is bacteriostatic in a concentration of 1-1 million against gram-positive organisms and in a concentration of 1-10,000 against gram-negative organisms. Referring to the gentian violet treatment itself, Aldrich states that in the two years following the introduction of this mode of burn therapy into the Johns Hopkins Hospital the mortality dropped from 42 to 13 per cent. Continuing with regard to the new dye combination, Aldrich says: "While the new dye is as superior to gentian violet as gentian violet is to tannic acid, I do not believe that it is the final answer to all the problems presented by a burned patient. I am certain, however, that the conception of a burn as an infected surgical lesion is correct, and that it is infection rather than absorption of a split protein which causes death in burns. For, let me add again, where there is no infection, there is no toxemia."

4. *Acriflarinc*.—This substance is used by Robertson,<sup>202</sup> 1933, in a 1-800 solution and by Mummery,<sup>203</sup> 1933, in a 1-1000 emulsion in medicinal paraffine.

5. *Mercurochrome*.—This substance was used by Sorrel, Guichard, and Gigon,<sup>204</sup> 1935, and by Turner,<sup>205</sup> 1935. The latter author states that tannic acid is bad because: (a) the coagulum is not transparent so that pus can form beneath without being seen, resulting in destruction of

that the speed of coagulation is very important from the standpoint of comfort and prevention of absorption.

III. *Saline Soaks*.—Blair and Brown,<sup>188</sup> 1931, and Blair, Brown, and Hamm,<sup>189</sup> 1932, have brought attention to the use of saline soaks rather than any chemical or precipitant treatment of burns. They point out that complete fixation retards the natural sloughing off of the dead tissues and thus delays the opportunity for surgical repair, and that caring for these wounds without resorting to tanning may require painstaking extra work, but it will be necessary for a shorter time and will win more worthwhile results. Plain water, physiologic solution of sodium chloride, or a mild antiseptic may be used, but a hypertonic salt solution seems to have special virtues. The soaking is usually done in a bathtub and the authors state that by its use most burned areas can be made sufficiently clean and the granulations sufficiently firm for grafting within from three to five weeks. Crile,<sup>190</sup> 1936, also uses the saline soak method. The excellent results from the standpoint of the eventual plastic result achieved by these men would suggest that it be used much more extensively and that it replace tannic acid in many instances. However, as the author<sup>124</sup> has pointed out, there are certainly some severe burns in which the immediate survival of the patient is of more imminent importance than the perfection of the ultimate plastic result, and in these instances, whether its action be by precipitating toxins or by preventing fluid loss, a tanning treatment does seem to reduce the immediate mortality. Furthermore, hypotonic soaks may be dangerous.

IV. *Other Methods of Burn Treatment*.—Some of these are modifications of the tanning method and others are not. The former will be considered first.

A. *Cutch Extract*.—Seeger,<sup>191</sup> 1935, advises a 5 per cent solution of Cutch extract which contains 60 per cent tannin and is less expensive than tannic acid. This author states in the same article that tannic acid (or Cutch extract) reduces pain, but "we have noted no reduction in mortality attributable to its use."

B. *Taktocut*.—The Jägers,<sup>192-194</sup> 1936, 1937, use taktocut, a somewhat similar tanning agent. In their hands this method has produced good healing without infection.

C. *Ferric Chloride*.—This method was used by Henry R. Slack,<sup>195</sup> 1915, of Lagrange, Ga., for a number of years, but it was never published by him. Slack found that when applying the tincture with applicators to the burned area, at first the alcohol caused more pain, but, as soon as the astringent effect occurred, the pain ceased. The application was repeated on return of the pain. The method was published independently by Coan,<sup>196</sup> in 1935 and now has some vogue. Coan uses the tincture or a 5 per cent solution.

D. *Gentian Violet and Other Antiseptics*.—These usually give an eschar that is more pliable than that produced by tannic acid and they

lor,<sup>178</sup> 1936) and the experimental work of Harrison and Blalock,<sup>92</sup> 1932, who showed that burned animals are more likely to die if débride-ment is performed.

I. *Ultraviolet Light*.—Trusler,<sup>223</sup> 1935, believes that ultraviolet light prepares the granulations for skin grafting and uses the light as an adjunct to other treatment.

J. *Picric Acid*.—Because of its poisonous properties, this is not used in the treatment of extensive burns at present, being entirely supplanted by tannic acid. However, in the form of an ointment, such as butesin picrate, it can be used to advantage on small burns. Christopher,<sup>224</sup> 1928, advises its use in such cases.

K. *Other Methods*.—In a study of the method of treatment of 752 cases of burns, Willems and Kuhn,<sup>225</sup> 1936, listed forty-seven different methods. Of these, forty have not been listed elsewhere in the present paper. Since these burns occurred from 1932 to 1934, they represent a diversity of method of recent times. This very diversity may mean either that no one treatment is suitable to all cases, that the ideal method has not yet been found, or that the general medical practitioner is not yet informed of the best methods. A few of the various treatments listed by Willems and Kuhn include unguentine (44 cases), antipyraxol (35 cases), boric ointment (25 cases), picric acid (18 cases), zinc oxide ointment (18 cases), carofax (4 cases), onol (3 cases), ambrine (3 cases),\* etc. It is quite possible that many of these were minor burns.

L. *Horse Serum*.—Introduced by Robinson,<sup>227</sup> 1917, and used more recently by Monteith and Clock,<sup>228</sup> 1929.

#### PATHOLOGY

I. *Local and General Changes*.—Inouye,<sup>67</sup> 1933; Fritz,<sup>229</sup> 1934; Dohrn,<sup>230</sup> 1901; Weimann,<sup>231</sup> 1927; and Schridde and Beekmann,<sup>232</sup> 1924, present data on pathologic findings. Bancroft's article,<sup>9</sup> 1937, in *Nelson's New Loose-Leaf Surgery* is a comprehensive review with illustrations. Hirota,<sup>233</sup> 1934, burned the hind legs of fifty-seven rabbits and made necropsy studies. He observed nuclear changes in the adrenals and alterations in the liver and kidneys. An extensive review of pathologic changes is given by Pack,<sup>234</sup> 1926, and some of the chemical aspects are discussed by Wells,<sup>235</sup> 1918.

II. *Blood Chemistry Changes Produced by Burns*.—According to the physical theory of production of shock in burns, the minor qualitative changes in the various blood constituents are of less importance than is the quantitative reduction in the amount of blood as a whole. This is said to be caused by a loss of plasma, and the fact that albumin may be

\*The ambrine treatment introduced during the war is seldom used nowadays. It is mentioned by Willems and Kuhn,<sup>225</sup> 1936, as being used in three of their collected cases and is discussed by MacLeod,<sup>226</sup> 1918, in *Oxford Surgery*. Ambrine is a patented paraffin preparation.



skin islands; (b) the skin bed is damaged; and (c) it is unstable. He finds that the use of a 2 per cent solution of mercurochrome overcomes these difficulties.

6. *Silver Nitrate Plus Gentian Violet*.—Just as tannic acid was supplemented by silver nitrate, so Branch,<sup>206</sup> 1935, uses the latter with gentian violet. In a series of eighteen cases he says that his method does away with several of the disadvantages of tannic acid, namely, too tough eschar, prevention of movement, lack of prevention of infection and killing of skin islands when the tough eschar is removed surgically.

7. *Dichloramin-T*.—This antiseptic has been in use longer than gentian violet and is usually administered in conjunction with paraffined gauze, such as by Lee,<sup>207, 208</sup> 1920, 1923, and by Ravdin and Ferguson,<sup>7</sup> 1925.

Methods independent of the tanning principle include:

A. *Cod Liver Oil*.—This method was introduced by Lohr,<sup>209</sup> 1934, and used by Holmes,<sup>210</sup> 1937; Steel,<sup>211</sup> 1935; Stevenson,<sup>212</sup> 1935; and Chevallier, Carcassonne, and Luccioni,<sup>213</sup> 1937. The cod liver oil is applied in the form of a wet dressing and is supposed to be mildly bacteriostatic and stimulating to the growth of new epithelium.

B. *Initial Cold Water Treatment*.—This method is used in Seattle by Rose,<sup>214, 215</sup> 1936, 1937, who has cut his mortality in half by its use. The patient is placed in a bath of water at 70° F. on admission and over a period of three hours this is heated gradually to 98° F., following which the patient is treated in the routine manner with either tannic acid-silver nitrate or ferric chloride. Greeley,<sup>181</sup> 1936, states that in scalds, if cold water is thrown on immediately, the scald may not penetrate so deeply. It is to be remembered, however, that the cold water treatment is in opposition to the generally recognized mode of dealing with shock in severely burned patients and aside from its temperature, its hypotonic effect on a raw oozing surface may be dangerous.

C. *Paraffined Gauze*.—Used by Sherman,<sup>6</sup> 1918; Paravacini,<sup>216</sup> 1928; Lee,<sup>207, 208</sup> 1920, 1923; and others.

D. *Viscopaste Bandage*.—Robb,<sup>217</sup> 1935.

E. *A mixture of dextrose, levulose, and sucrose* has been used by De Whalley,<sup>218</sup> 1935.

F. *Camphorated Oil*.—Mc Inturff,<sup>219</sup> 1936.

G. *Amyl Salicylate*.—Stewart,<sup>220</sup> 1937, has used amyl salicylate for minor burns where toxemia and shock are not factors. Since the substance has no bactericidal qualities, it is mixed with an antiseptic, such as "abride" (a mixture of isomeric substituted phenols). Amyl salicylate can be used on infected burns and is preferable to other salicyl esters, although its bad smell is a definite disadvantage.

H. *Débridement*.—This method has been used by Ravdin and Ferguson,<sup>7</sup> 1925; Låwen,<sup>221</sup> 1936; and Arzt,<sup>222</sup> 1935. Opposed to this method are the ideas of those who believe that skin islands may be left (Tay-

nonprotein nitrogen and hypochloremia, but their results are not open to the criticism that blood concentration changes alone may account for their alterations as their protein analyses were done on plasma and cells with reduction in both instances. Douglas,<sup>10</sup> 1934, cites blood chemical changes following burns.

Mattina,<sup>248</sup> 1935, reports an increase in the concentration of the blood magnesium of six rabbits burned by thermocautery, boiling water, or paraffin. The increase began twenty-four hours following the burn, reached its maximum in ten days and returned to normal in forty days. Fazekas and Baesich,<sup>249</sup> 1934, report an increase in lipid bodies in the blood leucocytes beginning in five hours, reaching a maximum in twenty-four to twenty-eight hours, and returning to normal after five to six days or longer. In fatal cases these bodies increase up to twenty-four hours and an hour before death may suddenly drop to below normal in number. Slocum and Lightbody,<sup>250</sup> 1931, reported that in both normal and adrenalectomized rabbits the sugar and lactic acid concentration of the blood is increased following burns. Since the adrenalectomized rabbits also showed the rise, this is interpreted as indicating that adrenal hyperfunction is not a factor. Van der Hulst,<sup>251</sup> 1937, reported a decrease in the rapidity of sedimentation of red cells during the first twenty-four hours with marked increase thereafter. These changes were not due to infection or blood concentration. Fasal,<sup>252</sup> 1937, found a shift to the left and toxic granules in the leucocytes.

Analyses of the edema fluid that leaks out into the tissues after burns are of interest. The chloride content is a little higher than in plasma, the sugar and nonprotein nitrogen contents are about the same, and the protein content about 80 per cent of that of plasma (Beard and Blalock,<sup>134</sup> 1931; Underhill and Fisk,<sup>127</sup> 1930).

III. *Blood Concentration.*—One of the chief blood changes following burns is a blood concentration occurring soon after the injury and subsiding in a few days in cases with recovery. Following this an anemia develops due to the combined effects of loss of blood from the granulating area, poor nutrition, and internal destruction of blood. Early writers to report blood concentration included Baraduc,<sup>253</sup> 1862; Tappeiner,<sup>254</sup> 1881; and Hock,<sup>255</sup> 1893. Hemoconcentration was reported by Locke,<sup>256</sup> 1905. Of ten cases of burns at the Massachusetts General Hospital, Locke found a red count over 9,000,000 in four of them. Pfeiffer,<sup>86</sup> 1905, also noted hemoconcentration as did Underhill, Carrington, Kapsinow, and Paek,<sup>130</sup> 1923. These latter authors studied twenty-one persons burned in a New Haven theater fire with a hemoglobin from 117 to 209. Mc Iver,<sup>144</sup> 1933; Shimada,<sup>96</sup> 1934; Lambret, Driessens, and Cornillot,<sup>142</sup> 1937; Lambret and Driessens,<sup>24</sup> 1937; Weiner, Rowlette, and Elman,<sup>147</sup> 1936; Douglas,<sup>10</sup> 1934; all noted hemoconcentration in burned patients. Simonart,<sup>141</sup> 1928; Blalock and his associates,<sup>133</sup> 1931; and Harkins,<sup>124, 136-139</sup> 1934, 1936; have also noted hemoconcentration in experi-

lost in slightly greater quantities than globulin and sodium chloride to a larger extent than sugar depends merely on a somewhat selective permeability of the burned capillaries for smaller molecules. It is as though a city of a million population were literally decimated by an air raid, the average size and other characteristics of the populace remaining would be little altered in the aggregate compared to the great reduction in number of people. However, to carry the illustration further, it is true that warfare is often more lethal to adult males than others producing a qualitative alteration in the population as well.

Blood chemistry changes have been noted following burns, and to many they represent the cause rather than the result of the shock factors present. Davidson,<sup>3, 5</sup> 1926, 1927, made an extensive study of the chloride and protein metabolism in burns. He found a significant lowering of whole blood and plasma chlorides. This was believed due to a lowering of the plasma chlorides below the renal threshold rather than to a primary kidney change. Davidson also found a hypoproteinemia with especial reduction in the amount of albumin. Underhill and others,<sup>128</sup> 1930, also found a lowering of blood chloride (whole blood), while Mc Iver,<sup>144</sup> 1933, found normal plasma chlorides. It is to be pointed out in this connection that with such marked blood concentration and altered hematocrit and a difference in the chloride concentration of cells and plasma (vide Harkins and others,<sup>236-238</sup> 1929, 1931, 1932) a chloride study of both cells and plasma should be made in burned patients. Therefore, since the cells normally contain less chloride than plasma and since in burns the cells are increased, this would explain the finding of low whole blood chlorides on the basis of the hematocrit changes alone but would not account for the difference in the results on plasma chlorides reported by Davidson and Mc Iver. Baur and Boron's,<sup>239</sup> 1933, report of reduced low blood chlorides in five surviving men out of nine burned in an airplane accident is open to the same objection as is the work of many other writers.

Cicala,<sup>240-243</sup> 1935, working on rabbits, reported a decrease in the blood chlorides, and an increase in the nonprotein nitrogen. He believed that some of the increase in nitrogen is due to histaminelike substances. The creatinine and uric acid increased, the latter he believed being due to renal tubular damage secondary to traumatic shock. The reduced glutathione of the blood increased. Another Italian investigator, Titone,<sup>244</sup> 1936, also reported an increase of glutathione in the blood of experimentally burned animals. It is to be remembered that hematocrit changes alone may explain many of these changes in nonprotein nitrogen, etc., when done on whole blood. Christophe,<sup>245</sup> 1933, finds that the presence of albumin in the urine, increased nonprotein nitrogen, hypochloremia, and low A/G ratio become most marked ten days after experimental burns in dogs. Lambret, Driessens, and Malatray,<sup>246</sup> 1936, and Lambret, Driessens, and Warembourg,<sup>247</sup> 1936, have reported increased

states that convulsions are practically always fatal and albuminuria and persistent vomiting are ominous signs.

Tetanus has been frequently reported as a complication of burns. Newberger,<sup>262</sup> 1912, reported 2 personal cases and collected 47 from the literature. Of these 49 cases, 38 died, making a 77 per cent mortality. Fasal,<sup>263</sup> 1935, reported on the extensive burn material in the skin clinic of Vienna. Of 2,327 burn cases seen from 1905 to 1930, not a single one developed tetanus, but in both 1932 and 1934 there was one case and thus he believes prophylaxis is to be considered. Kudrinsky,<sup>264</sup> 1936, gave case reports of tetanus following burns. Willems and Kuhn,<sup>225</sup> 1936, stated that of 752 collected burn cases only 23 received antitetanic serum, but as none of the other 729 cases developed tetanus, the physicians in attendance on those particular cases evidently did not use poor clinical judgment in refraining from administering serum.

In many clinics, including that of the writer, it is the practice to leave the right lower quadrant free when taking skin grafts in burn cases. This is considered especially advisable in children in whom the appendix has not been removed. Rose,<sup>215</sup> 1937, reported a case in which appendectomy was performed through a ferric chloride eschar twenty-three hours after a burn of the abdomen and thighs. The wound healed without drainage and six weeks later that area was skin grafted along with the surrounding granulating region and the patient recovered.

Fat embolism is a rare complication of burns but Strassmann,<sup>265</sup> 1933, reported on 125 cases of fat embolism due to blunt force and 5 following burns. He quotes Carrara as saying that in 46 per cent of burn cases coming to autopsy fat emboli are found.

Globus and Bender,<sup>266</sup> 1936, reported an extensive study of severe burns in an eight-year-old boy leading to fatal disseminated toxic degenerative encephalopathy (disseminated sclerosing demyelination). Clavelin and Hugonot,<sup>267</sup> 1936, reported a case with late formation of edema. They attribute the edema to low plasma proteins resulting from albumin loss from the granulating surface. Froment, Thiers, and Brun,<sup>268</sup> 1936, reported a case of burns with resultant anuria, hypertension, and bradycardia. However, their patient was burned so slightly that the sequence of cause and effect is not definite. Massabuau, Laux, and Ginestié<sup>109</sup> 1935, reported a burn with jaundice occurring on the third day.

It is quite possible, as was discussed in the section on the bacterial theory of death following burns, that many of the complications of these injuries are secondary to sepsis. Pfaunder and Schlossmann,<sup>269</sup> 1935, mentioned several complications, e.g., hemoglobinuria. They quoted Kruse who reported encephalitis with acute hydrocephalus and amaurosis in a fifteen-month-old child the day following a second degree burn. Scarlet fever or typical scarlet-like exanthema with rise in temperature may appear after severe burns. Some (such as Leiner) are wont to

mental burns. Ravdin and Ferguson,<sup>7</sup> 1925, noted a hemoglobin of over 100 per cent in all but two of their clinical cases and the red cell count was proportionately increased. As previously mentioned, hemoconcentration also accompanies shock from other causes.

IV. *Curling's Ulcer*.—This complication of burns was described by Long,<sup>257</sup> in 1840, and by Curling,<sup>258</sup> in 1842. Since then sporadic reports of peptic ulcer following burns have appeared in the literature including recently the reports of Willems and Kuhn,<sup>255</sup> 1936; Wilson,<sup>17</sup> 1935; Glover,<sup>182</sup> 1937; Torchiana,<sup>259</sup> 1936; and Kapsinow,<sup>260</sup> 1934. The last named author attributes them to blood stasis and concentration with capillary oozing and rupture, while other authors believe them to be toxic in origin. Glover,<sup>182</sup> 1937, states that bleeding from a Curling's ulcer accounted for 4 per cent of his deaths. Four other patients developed ulcer without death, three being diagnosed by x-ray and one ulcer requiring late gastric resection. The author does not state how many of these ulcers might have existed before. However, the two deaths were in children and this practically precludes a preexisting ulcer.

Underhill, Kapsinow, and Fisk,<sup>125</sup> 1930, showed experimentally that in the production of a burn heat may penetrate the interior of the body to a degree sufficient to increase temporarily the temperature of the body cavities by several degrees. They regarded such an increase of temperature as sufficient to lead to local circulatory changes inducing the formation of ulcers, hemorrhages, etc., which from time to time have been ascribed to the effect of a burn toxin. It should be pointed out in this connection, however, that clinical cases of Curling's ulcer have been reported in which the abdomen was not burned. The only case of Curling's ulcer in the writer's series,<sup>124</sup> 1936, occurred in a patient with marked sepsis: a peritonsillar abscess, fever of 104° F. or more for six days before death, and thrombophlebitis of the veins of one arm. In such a case bacterial emboli are to be considered in the etiology.

V. *Miscellaneous Complications*.—Pack,<sup>261</sup> 1926, summarizes burns in various locations in this connection by saying: "Burns of the scalp are peculiarly susceptible to erysipelatous inflammation, but are not so often followed by cerebral mischief as one would think. When the burn is limited to the extremities or to the back, where the thick dorsal muscles serve as effectual protection to the subjacent viscera, the outcome is encouraging. However, burns of the abdomen, with the dangerous visceral proximity, have the highest mortality. Burns of the genitalia, the anterior thoracic surface and the face (over the area of trigeminal distribution) cause symptoms and dangers far out of proportion to their area allotment. Mucous membrane involvement, especially of the pharynx and larynx, adds to the gravity of the case. Burns of the flexor surfaces are more serious than on the extensor surface." Pack further

states that convulsions are practically always fatal and albuminuria and persistent vomiting are ominous signs.

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regard these all as true scarlet fever, since quite frequently an angina, raspberry tongue, and desquamation and even transmissions occur. The possibility of a toxic erythema due to resorption of poisonous products from the damaged skin is to be kept in mind.

VI. *Malignancy Developing as a Late Result of Burns.*—Treves and Pack,<sup>270</sup> 1930, have reported a large series of carcinomas developing in burn scars (Marjolin's ulcer) treated at the Memorial Hospital in New York. Of 1,091 squamous cell and 1,374 basal celled carcinomas treated during the twelve-year period, 1917 to 1929, 21 (2 per cent) of the former and 7 (0.3 per cent) of the latter followed burns. The average age of the patients as a whole was about fifty-nine years and was fifty-four years for the burn cases. However, the age of the scar is more important than the age of the patient, as one case burned at the age of three years developed carcinoma at the age of seventeen years. It is of interest that of the entire 28 patients with carcinoma following burns, not 1 was ever treated by skin grafting. In 9 patients with a known healing time, 3 never healed, and for the other 6 the average healing time was 805 days. The average age of the scar was 32.5 years. Stauffer,<sup>271</sup> 1928-1929, reported a man with skin carcinoma developing on the face thirty days after a burn. As he had precancerous lesions elsewhere, the burn may have been coincidental. Johnson,<sup>272</sup> 1926, reported 4 cases of carcinoma seen at the Steiner Clinic in one year. Three of these cases were four years, eight years, and two years respectively in healing. The fourth case never healed and wore a dressing for sixty-one years. At that time (previous to Treves and Pack's report), Johnson could find no record in the literature of basal celled carcinoma developing in burn scars. Harkins,<sup>124</sup> 1936, has recently reported 2 cases of sarcoma following burns.

#### PLASTIC AND LATE TREATMENT OF BURN ULCERS AND SCARS

A trend towards the adoption of the thick Thiersch or "thick split" graft advocated by Brown and Blair has been noted in recent reports,<sup>188, 189, 273-277</sup> 1929-1936. Many other writers favor the use of the Reverdin, "pinch," or small deep graft of Davis,<sup>278-284</sup> 1929-1934, and this graft is still used in many instances, especially for children,<sup>124</sup> 1936, or over extensor surfaces. Homogenous grafts,<sup>285</sup> 1937, are sometimes used as a temporary life-saving measure by Bettman,<sup>286</sup> 1938, the idea being that even though these grafts do not take they will act as a protective covering for a few days or weeks. Bettman says in this regard that there is general recognition of the fact that homogenous grafts do not take permanently. However, during the three to five weeks that the grafts are adherent, the covered area is cleared of infection and the patient is saved the disastrous effects of septic absorption from those areas. By the time the grafts come away, the patient's condition is so greatly improved that measures which were not thought of earlier may

now be carried out with safety. Whole thickness grafts have been used in the repair of scars to advantage by Padgett,<sup>287</sup> 1937, while Ashley,<sup>288</sup> 1937, has used discarded foreskins preserved in ice cubes. Goode,<sup>289</sup> 1935, takes the thick split graft of Brown and Blair and cuts it in pieces after placing it epidermal side down on gutta percha. These pieces, about 2 cm. square, are then applied, with the gutta percha still attached, to the burned ulcer in the same manner as are pinch grafts. This author treats the donor area with tannic acid and fastens large thick split grafts to the recipient area by plastering the margins with collodion.

The later treatment of burn scars and contractures by pedicle grafts and other plastic methods has been described in several recent publications,<sup>290-301</sup> 1924-1937.

#### RELATED THERMAL AND ACTINIC TRAUMA

I. *Freezing*.—Harkins and Harmon,<sup>302-306</sup> 1934, 1935, 1936, 1937, have shown that many of the changes following freezing are similar to those following burns. A marked exudation of plasma-like fluid into the local tissues occurs with thawing, resulting in blood concentration, lowered bleeding volume and decrease in arterial pressure. This condition may be so severe as to be related to death of experimental animals. In these experimental animals a marked prolonged hypothermia was noted of about the same degree as that reported by Reineke,<sup>307</sup> 1875, in human beings (24.0° C., 75.2° F.).

II. *Sunburn*.—This usually produces a first or even second degree burn over the entire exposed surface area, involving especially the extensor surfaces, and it may be serious in some instances.

III. *Roentgen and Electrical Burns*.—Davis,<sup>308-309</sup> 1933, has made an extensive study of these burns. He concludes that early and wide excision of deep burns caused by Roentgen rays or radium, with closure of the defect thus made by tissue shifting, offers the best method for elimination of pain, prospects for permanent healing, and safety from subsequent malignant degeneration.

Electrical burns are noted for their depth, sharing this characteristic with Roentgen burns. They may erode large vessels and cause delayed death by secondary hemorrhage.

#### COMMENT

From the mass of work published in the past ten years, much of which shows no uniformity of opinion, it is difficult to arrive at arbitrary conclusions. In review, however, it seems that after a severe burn a patient may be subject to some degree of psychic or primary shock which usually quickly passes away. Following this, from the second to about the forty-eighth hour, secondary shock may ensue with marked blood concentration. Accompanying this is a moderate alteration in some of the chemi-



cal constituents of the blood and a marked exudation of plasma-like fluid into the burned area and from the burned surface, with, in experimental animals, lowered blood volume, bleeding volume, and cardiac output. Whether this stage of shock with resultant lowered blood pressure is due to these physical changes or to the production of a toxin, there is no uniformity of opinion.

Irrespective of whether this secondary stage is due to the physical effects of local fluid loss or to the poisonous effects of toxin absorption, it seems advisable in serious cases to administer an eschar-forming type of treatment to the local lesion. Such local treatment will seal off the tissues and prevent fluid loss or toxin absorption. Along with the local treatment, the usual supportive measures against shock should be used. The use of adrenal cortical extracts and blood plasma transfusions are to be considered. The choice of local treatment lies between numerous tanning agents. If the ultimate plastic result is of prime importance and the burn is not severe enough to endanger the life of the patient, escharotics may be omitted and saline baths used instead. If one adheres to the bacterial theory of toxin production, an antiseptic may be combined with the escharotic or used as a mild escharotic.

The presence of infection, usually *Streptococcus hemolyticus*, is a factor in the morbidity in the third stage of burns from the second or third day on during the next few weeks, especially the first ten days. At this time, if the patient has recovered, fluid loss is no longer an important factor except in producing a type of nutritional edema. The blood now becomes dilute and transfusions are necessary to overcome anemia rather than to combat shock. Toxins may or may not play a rôle at this time.

In the fourth or healing stage of burns, early skin grafting is advisable and in this work the use of thick split grafts is favored in many of the most recent reports.

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## II. Theories as to Origin of Burn Shock

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#### *Local Treatment of Burns*

##### *I. Tannic Acid*

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## II. Tannic Acid—Silver Nitrate

(See also Glover.<sup>182</sup>)

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#### *Local Treatment of Burns*

##### *I. Tannic Acid*

(See also Davidson,<sup>1-5</sup> Wilson,<sup>14-20</sup> Rudler,<sup>117</sup> Clark and Cruickshank,<sup>121</sup> Harkins,<sup>124</sup> and Mitchiner.<sup>146</sup>)

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## III. Blood Concentration

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(See also Inouye.<sup>67</sup>)

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IV. *Curling's Ulcer*

(See also Wilson,<sup>17</sup> Harkins,<sup>124</sup> Underhill, Kapsinow, and Fisk,<sup>125</sup> Glover,<sup>182</sup> and Willems and Kuhn.<sup>225</sup>)

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V. *Miscellaneous Complications*

(See also Rose,<sup>215</sup> and Willems and Kuhn.<sup>225</sup>)

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VI. *Malignancy Developing as a Late Result of Burns*

(See also Harkins.<sup>124</sup>)

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*Plastic and Late Treatment of Burn Ulcers and Scars*

(See also Harkins,<sup>124</sup> Blair and Brown,<sup>188</sup> and Blair, Brown, and Hamm.<sup>189</sup>)

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particularly, when certain indications exist. A few patients were reported in whom the common duct was drained with a T-tube, but in whom all stones were not recovered from the common duct at the time of operation. In such cases an attempt should be made to encourage the passage of the stones in the common duct without another operation. A routine consisting of the administration of atropine and nitroglycerin, and the injection of warm olive oil and saline solution through the T-tube has been developed in order to encourage the passage of the stones through the sphincter of Oddi. If the stones found in the common duct after operation are proximal to the T-tube, the tube will obviously have to be removed before the stones can pass through the duct. On one or two occasions when the routine mentioned above was ineffective in obtaining passage of the stone, the common duct was irrigated with ether in an attempt to dislodge or break up the stone. In the case in which this method was attempted, the procedure was not effective, however. Cholangiography at the time of operation is advised to aid the surgeon in finding stones in the common duct.

**Dr. Charles W. Mayo, Rochester, Minn., A New Method of Repair of Complete Rectal Prolapse:** Attention is called to the fact that many cases of severe prolapse of the rectum are associated with a hernia of the median perineal type, and in which small intestine may herniate into the prolapsed rectum. In dealing with this type of complete prolapse, a low midline incision is made and the neck of the sac, through which the small intestine herniates into the rectum, is brought upward. The floor of the pelvis, which is very lax, is reconstructed and reinforced with fascia lata removed from the thigh. Care is taken not to apply sutures in the bladder wall. The sigmoid is anchored somewhat by suturing epiploic tags to stable structures.

**Dr. John Alexander, Ann Arbor, Mich., The Indications, Technique, and Results of Surgery for Bronchiectasis** (In the absence of the guest speaker, Dr. Alexander, this paper was presented by **Dr. Cameron Haight, Ann Arbor, Mich.**): The institution of conservative therapy is emphasized before the radical procedure of lobectomy is performed. Conscientious postural drainage, pneumothorax, and phrenic interruption were discussed as procedures to be used before lobectomy, but unfortunately such measures are rarely curative. Occasionally patients are made worse by phrenic interruption. Bronchoscopy is of great value in determining the presence of bronchial stenosis as an etiologic factor in the development or presence of bronchiectasis. The essayist has practically discarded thoracoplasty in the treatment of bronchiectasis. Lobectomy is indicated, particularly in the unilobar disease. The results of bilateral lobectomy are obviously not good; poor results have discouraged the author from its continuation. In bilateral bronchiectasis it is usually preferable to perform lobectomy on the bad side and to wait considerable time to see if conservative treatment of the less diseased lobe will not be effectual. Prophylactic lobectomy in mild bronchiectasis is not favored, chiefly because the mortality following lobectomy is not insignificant. The x-ray, utilizing the injection of iodized oil, is very useful. One lobe should be injected, and lateral as well as oblique views should be taken. The author favors the two-stage operation and calls attention to the lowering of mortality from 8 to 14 per cent down to 4 per cent by the delayed two-stage operation of Churchill. Eleven total pneumonectomies were performed in the author's clinic for disseminated bronchiectasis with five deaths.

**Dr. Casper F. Hegner, Denver, Colo., Some Points in Surgical Collapse for Pulmonary Tuberculosis:** Conservative measures, including pneumothorax, phrenic interruption, and scaleniotomy, should be considered before thoracoplasty is advised. The author is of the opinion that temporary phrenic interruption produced by crushing of the nerve should be utilized more often than it is. In discussion



# Review of Recent Meetings

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## REPORT OF THE FORTY-SEVENTH ANNUAL MEETING OF THE WESTERN SURGICAL ASSOCIATION, INDIANAPOLIS, IND., DEC. 3 AND 4, 1937

WARREN H. COLE, M.D., CHICAGO, ILL.

*(From the Department of Surgery, University of Illinois College of Medicine)*

**DR. LOUIS RASSIEUR**, St. Louis, Mo., **A Clinical Study of Congenital and Familial Hemolytic Icterus:** In a family consisting of mother, father, and three children, all except the mother suffered from familial hemolytic icterus. Because of jaundice, anemia, etc., the father had a splenectomy three years before he was married. He died at the age of thirty-seven years with uremic coma. All three children were girls. In the first child anemia, slight jaundice, and weakness appeared early. Examination of stomach contents revealed no free hydrochloric acid. Splenectomy was performed. Gallstones were present in the gallbladder. The second child presented similar manifestations, including stones in the gallbladder and absence of hydrochloric acid in the stomach contents. Platelets numbered only 28,000. Manifestations of the third child were similar to those of the other two. Platelets numbered 26,000, but they rose to 600,000 after splenectomy. Splenectomy was performed on all three children with relief of symptoms, but slight icterus persisted. In discussion **Dr. H. H. Davis**, of Omaha, Neb., called attention to the frequency of hemoclastic crisis following transfusion before splenectomy in patients with familial icterus. **Dr. G. M. Curtis**, of Columbus, Ohio, called attention to the fact that the disease is genetic, i.e., carried by the chromosomes.

**Dr. Charles B. Puestow**, Chicago, Ill., **Choledochostomy with Studies of Intra-ductal Pressure:** The essayist called attention to errors in diagnosis as one of the most common causes of poor results following cholecystectomy. Studies on intra-ductal pressure within the common duct in animals and human beings revealed a lowered pressure following cholecystectomy. This lowered pressure suggests that there was a reflex disturbance of the denervation of the sphincter of Oddi caused by the procedure of cholecystectomy. This finding of the lowered pressure within the duct was encountered in all of the patients reported in this series, upon whom cholecystectomy had been performed and the common duct drained. The hypothesis is suggested that the relief of symptoms following cholecystectomy may be due, in great part, to this relaxation following cholecystectomy. In a series of patients examined at autopsy the circumference of the common duct was larger in those upon whom a cholecystectomy had been performed. This finding has been reported by other authors, although it is not entirely consistent in animals. As yet there is no satisfactory explanation available to explain this dilatation of the common duct.

**Dr. R. Russell Best**, Omaha, Neb., **Cholangiography Demonstration of the Remaining Common Duct Stone and Its Nonoperative Management:** The fact that over one-third of the patients having gallstones in the common duct are not jaundiced is a factor which makes exploration of the common duct so important,

particularly when certain indications exist. A few patients were reported in whom the common duct was drained with a T-tube, but in whom all stones were not recovered from the common duct at the time of operation. In such cases an attempt should be made to encourage the passage of the stones in the common duct without another operation. A routine consisting of the administration of atropine and nitroglycerin, and the injection of warm olive oil and saline solution through the T-tube has been developed in order to encourage the passage of the stones through the sphincter of Oddi. If the stones found in the common duct after operation are proximal to the T-tube, the tube will obviously have to be removed before the stones can pass through the duct. On one or two occasions when the routine mentioned above was ineffective in obtaining passage of the stone, the common duct was irrigated with ether in an attempt to dislodge or break up the stone. In the case in which this method was attempted, the procedure was not effective, however. Cholangiography at the time of operation is advised to aid the surgeon in finding stones in the common duct.

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**Dr. Stuart W. Harrington, Rochester, Minn.,** *Pharyngoesophageal Diverticulum:* The term pharyngoesophageal diverticulum is a poor one since the condition is in reality a herniation of the pharynx. These diverticula usually are present on the left side. They are apparently of congenital origin. The frequency of esophageal diverticulum makes esophagoscopy advisable in all patients with dysphagia. In the series of 33 cases reported, the operation was performed in one or two stages. In the latter type of operation, the first stage consists of immobilization of the diverticulum through a long incision in the neck usually on the left side. The second stage is performed seven to thirteen days later. This adds to the safety of the procedure because the area is walled off by the granulation produced by the first operation. Feeding for several days is restricted to that effected by means of a nasal tube. In 25 patients upon whom a two-stage operation was performed, 6 had a postoperative fistula, 2 had a recurrence, and 21 had relief from symptoms. In 8 patients upon whom the one-stage operation was performed, no complications were encountered and all were relieved of symptoms. The point was made, however, that these statistics should not condemn the two-stage operation.

**Dr. Edgar L. Gilcreest, San Francisco, Calif.,** *Lesions of the Shoulder:* The author emphasized the fact that most of the patients complaining of pain in the shoulder in the absence of fracture suffered from extra-articular lesions and not from arthritis. Lesions consisting of fraying or rupture of the supraspinatus tendon are not uncommon. A great deal of the symptoms referable to the shoulder are related to the fact that the shoulder joint is now a weight-carrying joint rather than a weight-bearing joint. The grating or crepitus which can be demonstrated so commonly in patients complaining of pain is rarely due to arthritis, but usually due to fraying and roughening of the tendons. Lesions of the biceps and triceps tendons were included in this discussion.

**Dr. Kellogg Speed, Chicago, Ill.,** *Spondylolisthesis:* Displacement of a vertebra as encountered in spondylolisthesis may occur at any level, but usually it occurs at the level of the fifth lumbar vertebra and sacrum. The lesion is frequently traumatic, but it may be associated with incomplete fusion of the neural arch. The more conservative methods of treatment, including the use of braces, corsets, traction, etc., were discussed. Operative procedures consist primarily of attempts to obtain bony fusion by an anterior or posterior operation. The anterior approach is usually easier than the posterior. The procedure described by the author is to drill a hole through the fifth lumbar vertebra into the sacrum, and to drive a bone transplant obtained from the tibia into this opening. This transplant affords fixation and is effective in the treatment.

**Dr. J. Dewey Bisgard, Omaha, Neb.,** *Fractures Involving the Epiphyseal Cartilage:* In a résumé of 232 fractures the author noted that significant injury

to an epiphysis was inflicted in slightly over 20 per cent of the cases. Injury to the epiphysis is very apt to result in prevention of normal growth, even though reduction may be adequate. Occasionally growth is interfered with only on one side of the epiphysis, thereby producing a deviation type of deformity, toward the injured side. Such deformities do not manifest themselves for several months after injury. In about one-half of the cases suffering from epiphyseal injury the x-ray will reveal disturbance in growth in about half the cases.

**Dr. Eslie Asbury, Cincinnati, Ohio, Internal Fixation of Hip Fractures Without an Open Operation:** Attempt has been made to treat fractures of the hip by internal fixation without resorting to such radical procedure as the use of the Smith-Petersen nail. The method used by the author consists of the introduction of three or four Kirschner wires through the trochanter into the head of the femur. Patients treated by this method should not be allowed to bear weight on the extremity under four or five months. When fractures of the femur are treated by Kirschner wires, attempt should be made to obtain slight over-correction of the deformity. In 39 cases reviewed, 28 had union.

**Dr. James R. McVay, Kansas City, Mo., The Treatment of Diverticula of the Bladder:** The details of preoperative and postoperative treatment of diverticula of the bladder were presented. The diverticula were dissected out and the cut edges brought together with No. 00 chromic catgut. The bladder is kept empty with a retention catheter which is attached to a suction apparatus similar to Wangenstein suction. In discussion, **Dr. H. L. Kretschmer, Chicago, Ill.**, remarked that many diverticula need not be resected if the etiologic factor, which is usually an obstruction, can be removed.

**Dr. Henry McGraw, Denver, Colo., Intestinal Obstruction:** The author traced the development of the various procedures advised from time to time as supplementary aids in the treatment of intestinal obstruction. The use of Wangenstein suction has resulted in a lowering of mortality and the elimination of operation in the treatment of many cases. One of the dangers in the use of Wangenstein suction is that the surgeon may misinterpret the slight improvement which always follows the institution of Wangenstein drainage. If operation is necessary and is delayed, the mortality will obviously be increased. In discussion, **Dr. Thomas G. Orr, Kansas City, Kan.**, called attention to the fact that enterostomy is seldom used any more in the treatment of intestinal obstruction since it is not needed when drainage through the opening is effected and since it is of no value when no drainage is effected. **Dr. Urban Maes, New Orleans, La.**, reported a reduction from 60 to 30 per cent primarily because of the institution of Wangenstein drainage, but he said the mortality in his department was now increasing because of the false security.

**Dr. Claude J. Hunt, Kansas City, Mo., Pancreatic Cyst:** Historical data and the classification of pancreatic cysts were presented. It was emphasized that the cyst may present at varied positions with relation to the stomach. Symptoms are due to pressure and disturbed physiology. The x-ray should be of significant aid in establishing the tumor as arising from the pancreas. The case presented was treated by excision of the cyst, although this is by no means always possible.

**Dr. Frank C. Mann, Rochester, Minn., The Effect of Decreasing the Lumen of a Blood Vessel:** Various methods of measuring the rate of flow of blood through a blood vessel were discussed, paying particular attention to the method utilizing dissemination of heat. Unexpected results were obtained so far as considerable

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Dr. Hugh Trout, Roanoke, Va., showed a beautiful colored moving picture of the radical operation for carcinoma of the breast. The operation he uses is essentially the Halsted operation. He believes that irradiation should be used as an adjunct to surgery but that it has no replacement value for surgery.

Dr. Edgar L. Gilcreest, San Francisco, Calif., read a paper on lumbosacral and sacroiliac sprains, calling attention to the fact that back pain as a single entity probably causes more industrial disability than any other condition. The causes of back pain are numerous. Acute or chronic sprain is the most frequent cause. Infection is the next most frequent cause. Congenital anomalies, neuropathic condition, metabolic conditions, and neoplastic causes are less frequent. Protrusion of the intervertebral disk is a possibility which must be ruled out. Dr. Gilcreest paid particular attention to acute and chronic sprains and slips in the sacroiliac and lumbosacral regions. He outlined the clinical aspects and advocated heat and massage and manipulations, which consist of forcibly flexing the knee with counterforce on the shoulder while the patient is on his side, and flexing the leg with the patient on his back, the other leg hanging over the side of the table fixing the pelvis. Relief is prompt in a large percentage of patients after these measures.

Dr. Ralph G. Carothers, Cincinnati, Ohio, discussed internal fixation of fractures of the neck of the femur. Dr. Carothers had some helpful suggestions for doing the operation. He uses the Austin Moore method with variations. A towel clip at the middle of Poupart's ligament serves as a very helpful guide to the head of the femur. After reduction, anteroposterior roentgenograms with this clip in place and a lateral roentgenogram with the edge of the casset flat on the table give information in the former view of the accuracy of the towel clip as a guide and in the latter view of the inclination from the horizontal necessary to hit the head of the femur. Of 26 cases in which he used this method, 9 had intertrochanteric fractures and 17 had intracapsular fractures. Of the intertrochanteric fractures 8 had bony union and 1 died. Of 17 intracapsular fractures, 2 died early; 5 have bony union in good position; in 4 the neck was absorbed; 2 had union but also a limp; 1 died of pneumonia ten weeks after operation; 3 have been operated upon less than three months.

Dr. R. Arnold Griswold, Louisville, Ky., discussed the treatment of delayed union and nonunion of fractures by subcutaneous drilling. In 12 cases in the last two years, all of which had delayed union or nonunion of subcutaneous bones, Dr. Griswold performed multiple drillings in a fan-shaped manner through the two fragments. After this procedure, all obtained union. Dr. Griswold called attention to the fact that this relatively minor operation will often obtain the desired results without having to perform more radical surgery.

Dr. Frank Strickler, Louisville, Ky., attempted to find a more suitable material for internal fixation of the fractures. Chronicized beef tendon, which he has prepared specially, was found to be a very suitable material. It has a certain rigidity, but it is absorbed after approximately ninety days. It doesn't show in the x-rays. He showed various methods of using this material for fixation of fractures; as a cuff over the two fragments held by kangaroo tendon, as two pegs for intermedullary support, and other methods.

Dr. J. C. Gerster, New York, N. Y., reported a case of rupture of a diverticulum of the jejunum resulting in peritonitis. The patient's general condition permitted only drainage of the diverticulum. Death resulted later in the con-

decrease in the lumen of the artery could be effected without producing a decrease in the blood flow. The external diameters can be decreased as much as 50 per cent with a resultant decrease in flow of only 18 per cent.

**Dr. Everett P. Coleman, Canton, Ill., Injection of the Right Stellate Ganglion with Alcohol in Paroxysmal Tachycardia:** The stellate ganglion of a patient who had daily attacks of paroxysmal tachycardia associated with a diseased gallbladder was injected with alcohol. The history of cholecystitis was of twenty years' duration and the paroxysmal tachycardia of four years' duration, suggesting that there was little relationship between the two diseases. The injection of the alcohol produced almost an instantaneous cessation of the paroxysmal tachycardia, the heart rate dropping from 200 down to 88. The dangers associated with the injection were discussed.

**Dr. Gordon S. Fahrni, Winnipeg, Canada, Hyperparathyroidism:** Four patients with hyperparathyroidism were reported, paying particular attention to the author's last case in whom two tumors were encountered. In this patient one tumor was found embedded in a lobe of the thyroid; whereas, the other was found in the mediastinum. X-ray pictures of the bones were shown to illustrate the calcification occurring in the decalcified areas following excision of the tumor. The importance of the laboratory data was stressed.

**Dr. William T. Peyton, Minneapolis, Minn., Hemangioma and Its Treatment:** The author emphasized that many cavernous hemangiomas need not be excised but could be eliminated by the injection treatment. The injection treatment recommended consisted of several injections of not more than 3 c.c. of sodium morrhuate into the tumor. A comparison of results in patients treated with radiation and those treated with injection revealed a cure in about 55 per cent and 82 per cent, respectively.

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## REVIEW OF THE SOUTHERN SURGICAL ASSOCIATION MEETING, DEC. 7-9, 1937, BIRMINGHAM, ALA.

HOWARD R. MAHORNER, M.D., NEW ORLEANS, LA.

*(From the Department of Surgery, Tulane University School of Medicine)*

THE fiftieth annual meeting of the Southern Surgical Association was held in its nativity city, Birmingham, Ala., at the Tutwiler Hotel, December 7, 8, and 9. One hundred forty-nine members were present. Of forty papers on the program thirty-eight were presented.

**Dr. Isidore Cohn, New Orleans, La.,** discussed malignant disease of the breast in negroes. At the Charity Hospital in New Orleans from 1932 to 1936 inclusive there were 408 cases of carcinoma of the breast in white and colored races. Two hundred and fifty-six of these were in the colored race. The incidence of 1.7 per 1,000 admissions has been a fairly constant rate during this time without annual variation. The average age for the colored patient was 4.7 years younger than was average age of the whites. The average duration of symptoms was 1.6 years. Of 224 colored patients in whom the records were sufficiently complete for such study, 118 had radical operations. Sixty-three of these had glandular involvement; that is, 60 per cent had axillary involvement on admission. The mortality after operation is approximately 65 per cent in from one to four years.

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**Dr. Edward H. Ochsner**, Chicago, Ill., reported an interesting case of simple nonparasitic cyst of the liver. Such cysts are extremely rare, are more common in women, and occur at the anterior margin of the lower surface of the liver. In his case the cyst of the liver contained four gallons of murky fluid. The wall was partially removed at operation and the remaining wall was marsupialized. Microscopic section showed columnar epithelium. The patient made an uneventful recovery and at a subsequent operation for another cause some years later there was no evidence of the cyst except adhesions from the region of the liver to the abdominal wall.

**Dr. R. L. Rhodes**, Augusta, Ga., discussed acute cholecystitis. He believes that more attention should be paid to an analysis of the blood chemistry in these cases. Blood sugars, blood chlorides, and nonprotein nitrogen and uric acid determination are all important and preliminary preparation of the patient should be directed in some measure to elevation of lowered blood sugar and chlorides and to reduction of elevated nonprotein nitrogen. In discussing this paper, **Dr. Charles Gordon Heyd**, New York, N. Y., emphasized the necessity of reestablishing diminished liver function. He believes that drainage of gallbladder facilitates drainage of the liver.

**Dr. William B. Marbury**, Washington, D. C., discussed retroperitoneal (retrocolic) appendix. The condition is not extremely common, but it does occur where the appendix in its embryonic descent gets caught under the colon and becomes entirely retroperitoneal. The clinical appearance is apt to differ from that of typical acute appendicitis in that the pain is not localized definitely at McBurney's point. The tenderness is higher and more posterior. Blood or pus may be found in the urine. **Dr. Marbury** reported 6 cases. The operation is sometimes difficult because the appendix is hard to find. It may be traced by first identifying its base at the ends of the longitudinal bands on the cecum.

**Dr. Vernon Mastin**, St. Louis, Mo., in an extensive study based on records of 9,592 patients having operations showed that preoperative medication definitely influenced the incidence of postoperative complications. Of 7,901 abdominal operations, 5,324 received morphine and atropine preoperatively; 2,318, morphine and hyoscine; and 259, morphine and barbiturate. In the morphine and atropine group 2.7 per cent developed cystitis or pyelitis; in the morphine and hyoscine group, 13.7 per cent; and in the morphine barbiturate group, 2.3 per cent. Studies for other operations and complications showed similar incidences. Morphine and a barbiturate administered preoperatively is followed by fewer complications than the other two combinations.

**Dr. R. Glen Spurling**, Louisville, Ky., has sectioned the scalenus anticus muscle in 20 cases for neurocirculatory compression without cervical rib. Of 17 cases which he was able to follow, relief of symptoms had been complete in all except 3. In these 3 there had been improvement. The symptoms of this syndrome, which was first recognized by Naffziger as occurring independently of supernumerary rib, are pain in the distribution supplied by the brachial plexus, numbness or hyperesthesia, muscular weakness, diminution in pulse, especially when the patient turns the head to the affected side and takes a deep inspiration, and tenderness over the scalenus muscle. The condition is not rare and better appreciation of the symptoms and diagnostic signs will result in more cases being recognized.

**Dr. Charles Bagley, Jr.**, Baltimore, Md., reported 2 cases of gas bacillus infection causing brain abscess. He found only 20 proved cases of this type in the literature. One of his cases was due to a puncture wound, the second to



valescence from uremia. Other than Meckel's diverticulum, diverticulosis of the colon is most common, next diverticulosis of the duodenum, and lastly single and multiple diverticulosis of the jejunum. The author's case had nine diverticuli, one of which had ruptured. From the literature he collected 186 cases in 129 references. A large percentage of diverticula of the jejunum give no symptoms. Others give flatulent dyspepsia and others symptoms of chronic intestinal obstruction. Occasionally rupture occurs.

**Dr. Vernon C. David**, Chicago, Ill., read a most instructive paper on the influence of diverticulitis on the mortality associated with surgery of the colon. Numerous complications occur from diverticulitis of the colon. Adhesions resulting from diverticulitis may seriously interfere with resection of the colon for carcinoma. Inflammation of sigmoid diverticula may result in adhesions to adjacent organs, notably the bladder. Appendices epiploicae may contain diverticula and for that reason are not to be ligated. In 5 instances he has noted abdominal wall infections from perforation of a diverticulum on the loop of a colostomy. In his experience perforation of a diverticulum resulted once from colonic irrigation, twice from obstruction. In 2 instances he found pylophlebitis caused by diverticulitis.

**Dr. Henry W. Cave**, New York, N. Y., discussed the surgical treatment of intractable chronic ulcerative colitis. In those instances in which medical measures have failed and the disease has persisted in a severe and intractable form, the only hope of cure lies in eradication by total, or in the segmental form by partial, colectomy. In his experience appendectomy, cecostomy, and colostomy have no place in the treatment of this disease as they are intended to permit irrigations which are not effective. After careful preparation of the patient, colectomy is performed in three or four stages. Ileostomy as the preliminary step is essential. Five weeks later, colectomy, removing the ascending, transverse, descending, and part of the sigmoid colon. Two to six months later combined resection of the remaining colon and anus is performed. He has performed 6 colectomies with no deaths. After colectomy the terminal ileum assumes the functions of the colon to a certain extent and the discharges become less fluid, but this transition of function in the ileum occurs only after the colon has been removed.

**Dr. John Gerster**, New York, N. Y., in discussing Dr. Cave's paper, said that one of his patients had had a cecostomy for ten years and wanted this cecostomy closed as the ulcerative colitis seemed to be dormant. X-ray, however, showed a colon with the lumen almost obliterated, the barium showing in parts as only a thin line.

**Dr. Fred Rankin**, Lexington, Ky., president of the Association, discussed this paper in some detail. He called attention to the fact that ileocolostomies and subtotal colectomies are rarely indicated because segmental involvement is rare.

**Dr. Arthur W. Allen**, Boston, Mass., gave a splendid paper on carcinoma of the stomach with special reference to total gastrectomy. At the Massachusetts General Hospital there have been 713 cases of carcinoma of the stomach. One hundred and seventy-six of these were subjected to subtotal gastrectomy and 13 to total gastrectomy. Two additional cases had total gastrectomies for other reason than carcinoma. He advocates anastomosis of the long loop of jejunum to the end of the esophagus, anchoring the jejunum to the diaphragm, an enterostomy at the dependent portion of the loop of jejunum, and a jejunostomy distal which is brought out of a side stab wound for feeding. In this series of 15 patients, 7 are dead; 2 are alive without recurrence, 1 twelve months and 1 four years after operations.

**Dr. Addison G. Brenizer**, Charlotte, N. C., demonstrated excellent results obtained by the use of an original method of fascial implants in the repair of harelip and cleft palate.

Discussing Dr. Brenizer's paper in which Langenbeck's operation was mentioned, **Dr. H. J. Boldt**, New York, N. Y., treated the assembly to some historical reminiscences. When he was very young, having suffered a broken arm, he was a patient of the great Langenbeck. He stated that in convalescence Langenbeck each day had him go to the abattoir's and take two types of baths, the so-called "blood bath" in which he immersed his arm in a bucket of fresh beef blood for half an hour, followed by an "intestinal bath" in which he bathed his arm in the opened abdominal cavity of a freshly killed beef for half an hour. He thought it would be interesting for the members to know how the old methods contrast with the new.

**Dr. J. Barrett Brown**, St. Louis, Mo., showed beautiful results obtained by grafts in surface defects of the hand. Full thickness grafts were more frequently used; occasionally a pedicle graft was used. Careful dissection of scarred tissue and meticulous attention to detail were stressed.

**Dr. Lawrence R. Wharton**, Baltimore, Md., described a new technique of reconstructing the vagina and reported its successful use in 4 cases. The technique consists of making a stent, or mold, of balsam wood covered by rubber which is inserted after dissection between the rectum and bladder in the normal location of the vagina. The stent is left in for approximately three weeks and epithelium grows in from the surface to completely line this new cavity which retains its adequate size. Microscopic sections of the wall of these patients have been taken and are found to be entirely healed over with stratified squamous epithelium.

**Dr. R. L. Sanders**, Memphis, Tenn., discussed cysts of Gartner's duct. He reported a case of a large cystic mass occurring in the anterior vaginal wall and protruding from the introitus which initially looked like a prolapse but proved to be a cyst in the anterior vaginal wall. It extended on over to the wall of the bladder, was successfully removed at operation, and contained a thin mucilaginous fluid. Its location and pathologic characteristics proved it to be a cyst of Gartner's duct.

**Dr. William T. Black**, Memphis, Tenn., reported 3 cases of hernia through the posterior vaginal wall. This is a true hernia, has a sac, and is to be differentiated from rectocele, with which it might be confused to the great regret of a surgeon. One of his patients was nulliparous; 1 case occurred after trauma. Treatment consists in isolation of the sac, excising it and repairing the defect.

**Dr. W. D. Haggard**, Nashville, Tenn., in discussing this paper, stated that he had had one such case which he had cured by opening the sac and packing the culdesac from below with gauze, thus producing adhesions which cured the hernia.

**Dr. William E. Lower**, Cleveland, Ohio, reported an interesting case of diverticulum of the urethra in a woman. Such a possibility is to be kept in mind in instances where there is prolonged urinary frequency or dysuria. Diagnosis is made by urethroscopy, probing the diverticulum, and injection of a radiopaque medium. Treatment consists in complete excision and primary closure of the urethra.

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a compound fracture resulting from a blow with a stick. Both recovered. One, however, developed tetanus during convalescence, and under huge doses of serum and avertin to control convulsions the patient recovered.

Dr. Mims Gage, New Orleans, La., gave a very complete discussion of pilonidal sinus. Differentiating it from sacrococcygeal dimple, he discussed the various etiologic possibilities and why the evidence is greatest in favor of the condition being a remnant of the neurenteric canal. Among important points in the treatment of the condition are accurate localization of the sinus by lipiodol injection and x-ray and by preliminary injection of the sinus on the fifth, fourth, and third days preceding the operation with methylene blue to stain the tract. The sinus is excised completely and primary closure is made, obliterating the dead space with sponge pressure. All 42 cases healed without recurrence.

Dr. L. Wallace Frank, Louisville, Ky., discussed thoracoplasty in the treatment of tuberculosis with special reference to the Semb procedure. Dr. Frank believes that the Semb operation is an epochal advance in the treatment of tuberculosis as it permits release of the apex and closure of cavities with resection of a minimum number of ribs, thus preserving more of the normal lung and accomplishing with greater certainty closure of cavities than by other methods of thoracoplasty.

Dr. Byrd C. Willis, Rocky Mountain, N. C., reported 104 cases of empyema in children occurring in years 1915 to 1937. There were 5 deaths. There were 79 cases under eleven years of age with 4 deaths. All cases are treated by interrib puncture with trocar and insertion of a tube. Careful attention to the after-care is necessary, being sure that drainage continues satisfactorily by persistent irrigations. No chronic empyemas developed. The procedure has the advantage of being a relatively simple method of obtaining satisfactory drainage. A minimum scar is left.

In discussing this paper, Dr. James Mason, of Birmingham, Ala., said he had employed rib resection on a similar group of cases with 1.6 per cent mortality. Other discussions showed differences of opinion on the method of obtaining drainage, but all agreed that different methods with careful attention to detail would accomplish satisfactory end-results. In discussing this paper, Dr. George A. Hendon, of Louisville, Ky., stated that he had used effectively warm air passed over iodine with which to irrigate the empyema cavity.

Dr. James D. Rives, New Orleans, La., read a paper on pulmonary abscess and discussed the factors influencing mortality. In 239 cases occurring in Charity Hospital from 1929 to 1936 and at Touro Infirmary from 1926 to 1936, there were 100 deaths. The mortality was higher before ten (52 per cent) and after forty years of age. The known mortality in this series is 42 per cent. One hundred and ninety-six of the cases were treated medically with a mortality of 44 per cent and 43 per cent were treated surgically with a mortality of 33 per cent. He does not believe duration of abscess is an important factor in the mortality. However, the amount of lung involvement is a very important factor. Single abscesses resulted in the 28.5 per cent mortality; bilateral abscesses, in 93 per cent; multiple abscesses in a single lobe, in 57 per cent; and abscesses in multiple lobes in one lung, in 45 per cent mortality. Of the 100 fatal cases only 23 cases had extrapulmonary and extrapleural complications. He believes that surgical treatment is indicated in abscesses located peripherally and in cases which do not respond to conservative measures. Aspiration of the abscess and artificial pneumothorax have no place in the treatment of this condition.

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**Dr. Curtis Tyrone**, New Orleans, La., read a paper on the comparative study of three types of hysterectomy. Of 764 hysterectomies performed by the late great **Dr. C. J. Miller** and himself in the years 1930 to 1936, inclusive, 316 (40 per cent) were supravaginal hysterectomies; 137 (20 per cent), complete abdominal hysterectomies; 311 (40 per cent), vaginal hysterectomies. The causes for hysterectomies were fibroids in 382 cases; fibrosis and chronic metritis in 238 cases; and pelvic endometritis in 74 cases. Other causes were present in the remaining cases. The operative time is no factor in determining which operation to use, because the difference in the average time necessary to perform each of the three types of operations is not greater than five minutes. He reported the commendable mortality of 1.9 per cent for supravaginal hysterectomies; 2.2 per cent for complete abdominal hysterectomies; and 0.64 per cent for vaginal hysterectomies. Combined mortality was 1.4 per cent.

**Dr. Walter E. Dandy**, Baltimore, Md., reported a case of an intracranial aneurysm which he first saw soon after its initial symptoms. Exploration revealed a small aneurysm of the circle of Willis, which had ruptured and formed a small false sac and which was pressing on the third nerve. He put a silver clip around the neck of the aneurysm sac and fulgurated the aneurysm itself. Complete cure resulted. Not all aneurysms at this location are amenable to surgical treatment because of (1) the difficulty of diagnosis and (2) the difficulty of approach of certain arteries.

**Dr. Rudolph Matas**, New Orleans, La., discussed **Dr. Dandy's** paper. He reviewed in great detail the problem of aneurysms of the circle of Willis and stated that this was the first true arterial aneurysm of the circle of Willis which had been cured by occlusion. He believes that cranial encephalography opens great possibilities for diagnosis of these conditions.

**Dr. Waltman Walters**, Rochester, Minn., reported 7 cases of suprarenal cortical tumors in which operation had been done and in which recovery followed. He emphasized the difficulty of differentiating between adrenal cortical tumors and pituitary basophilism. Adrenal cortical tumors may mask under clinical characteristics similar to those of pituitary basophilism and, therefore, doubtful cases should have the advantage of an exploration of the adrenal glands. Not all tumors of the adrenal glands produce typical virilism or changes in the secondary sex characteristics. In some instances the changes are very mild and because these tumors tend to be malignant early diagnosis is imperative. Recovery in 7 consecutive cases he attributes to increased knowledge of the disturbed physiologic processes and to better postoperative care. This consists of administration of large amounts of sodium chloride and sodium citrate and the daily administration of an adequate amount of cortical hormone in the immediate postoperative period.

**Dr. Loyal Davis**, Chicago, Ill., discussed the surgical problem of hypertension. **Dr. Davis's** indications for surgery in essential hypertension are extremely rigid. He accepts only those cases which have a potentially reversible blood pressure and which, on the other hand, do not respond to medical management and administration of cyanate. The pressure must be above 200 systolic and 100 diastolic and there must be no evidence of renal impairment due to glomerular damage. Thus, he has had a small number of patients in which he has done a combined sympathetic and splanchnic resection by the transthoracic method advocated by **Pret**. Of 6 patients operated upon, all have returned to their preoperative blood pressure levels within ten days. On the other hand, he had another patient who was operated upon elsewhere and after returning to him, though the pressure had reached its

previous level, the patient responded to cyanate therapy. In an additional case of his own the patient became sensitive to cyanate therapy after operation. Although the operation may not accomplish all that has been hoped, it may change the patient's response to cyanate, thus opening new possibilities for alleviating the condition.

**Dr. George Crile**, Cleveland, Ohio, prefers to remove the hypogastric plexus for essential hypertension. He has found operations on the sympathetic system helpful in neurocirculatory asthenia, recurrent hyperthyroidism, and hypertension and such vascular conditions as Raynaud's disease. He considers the adrenals and hypogastric plexus together as an organ which is an energy arsenal for use in emergency. As might be suspected, the lion, which has the most tremendous burst of energy, has relatively the largest adrenals and hypogastric plexus. In 213 cases of hypertension, after removing the hypogastric ganglia, at least symptomatic benefit has resulted in approximately 90 per cent of the cases.

**Dr. Howard R. Mahorner**, New Orleans, La., discussed the modern treatment of varicose veins. In a test devised by himself and **Dr. Alton Ochsner**, New Orleans, La., it is possible to determine the exact level of leaks from the deep to the superficial system in the varicosed extremity. In those instances in which the valves of the saphenous vein alone are incompetent, high ligation of the saphenous with injection of a sclerosing solution in the distal stem results in a cure. However, in those instances in which the comparative tourniquet test shows incompetence of valves of the communicating veins as well as incompetence of the valves of the saphenous, not only high ligation of the saphenous is done, but also low ligation to reduce the retrograde flow from the deep to the superficial system. A moving picture demonstrating the test and treatment was shown.

**Dr. Hugh Gamble**, Greenville, Miss., reported a new operation for tracheoesophageal fistula and reported a case of tracheoesophageal fistula occurring in the newborn. He divided the stomach at the cardiac end, closed the distal part, and made a gastrostomy. The proximal end, which was attached to the esophagus, was brought out through the abdominal wound permitting free drainage of the esophagus. The patient lived for fifteen days and died of peritonitis due to a rupture of an ulcer of the stomach.

**Dr. K. H. Aynesworth**, Waco, Tex., discussed pain in acute abdominal surgical emergencies. After reiterating the various theories relative to the transmission of pain from abdominal organs, evidence was advanced for accepting the theory that pain is transmitted by cerebrospinal nerves and not by sympathetics. Anatomic structure and disturbed physiology determine the type of pain, and the character and location of the pain are helpful guides to the correct diagnosis. The relationship of local and referred pain to various pathologic processes in the abdomen was considered in detail.

**Dr. W. O. Bullock**, Lexington, Ky., advocated the use of glass rods over which mattress sutures are tied to prevent disruption of a laparotomy wound in cases which have to be drained.

**Dr. Charles E. Robins**, Richmond, Va., presented an operation for the cure of direct inguinal hernia. Dr. Robins drew attention to the fact that that part of a conjoined tendon which is usually attached to Cooper's ligament is frequently deficient in patients with indirect inguinal hernia. Dr. Robins' operation consists of inserting a fascial suture, beginning at the firm suprapubic ligament, catching the edge of the rectus fascia, sewing it down over the cord to Poupart's ligament,

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# Book Reviews

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**Diseases of the Nervous System in Infancy, Childhood and Adolescence.** By Frank M. Ford. Pp. 953, with 107 illustrations. Springfield, Ill., and Baltimore, Md., 1937, Charles C. Thomas, Publisher. \$8.50.

This is an accurate and comprehensive text, perhaps somewhat voluminous (953 pages) but almost necessarily so if the subject is to be presented well and brought up to date, as the author has done. Illustrative case histories throughout the text comprise approximately 100 pages. The reviewer personally feels that case histories are unnecessary in a well-written text, such as this one is, and therefore that the book might have been shortened, to the extent of omitting these pages, without detracting from its subject matter.

The first two chapters (148 pages) deal with the examination of the nervous system and the clinical aspects of the anatomy and physiology of the nervous system. In the succeeding chapters the author presents the diseases of the nervous system according, as he states in the preface, to a classification based primarily upon etiology with due emphasis upon clinical features, rather than upon a purely anatomic classification as is customary. This classification improves one's understanding of these diseases. The individual diseases are discussed both intelligently and intelligibly.

Following the discussion of each disease entity is a brief but carefully chosen bibliography. In the selection of the references the author favored those which are written in English and which are easily available.

There are not many cuts for so complete a book but those pictured are clear and illustrative. The print, paper, and binding are all of very good quality.

The book is a medical rather than a surgical treatise; hence it is of most value to the neurologist and pediatrician, but valuable also to the neurosurgeon and in fact to any doctor of medicine. The reviewer, a neurologist, thoroughly enjoyed the book and commends the author upon his excellent work.

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**Genital Abnormalities, Hermaphroditism, and Related Genital Abnormalities.** By Hugh H. Young. Cloth. Pp. 649, with 379 illustrations. Baltimore, 1937, The Williams and Wilkins Company. \$10.

The scope of this interesting and valuable volume is not fully indicated by its title, since it covers not only hermaphroditism and pseudohermaphroditism and abnormalities of the male genitalia, but also disturbances of the endocrine glands which influence the sex organs and characteristics. It contains both a thorough-going review of the literature and a detailed discussion of Dr. Young's extensive experience. It is profusely and excellently illustrated.

The discussion of hermaphroditism in literature and art, the review of the embryology of the condition, and the engaging presentation of case histories of hermaphroditism and the much commoner pseudohermaphroditism make it an abbreviated counterpart of Neugebauer; but the discussions of the rôle of the endocrine glands in the production of these and related conditions, as well as the admirably illustrated descriptions of the operations required for their correction, make the scope of this book much greater than that of Neugebauer's.



continuing in this plane suturing the fibers of the internal oblique and transversalis muscles to Poupart's ligament. The aponeurosis of the external oblique is sutured over this. This supplants the deficiency in the conjoined tendon in these cases.

**Dr. Carrington Williams**, Richmond, Va., advocated the use of an abdominal approach in the repair of inguinal hernia; (1) in cases with strangulated hernias, (2) where it is desirable to remove the appendix at the same operation, (3) for sliding hernias, (4) for congenital hernias, and (5) for cases in which there is an undescended testicle. The usual oblique incision is made, but after incising the aponeurosis of the external oblique a split-muscle incision is made above the level of the internal ring. The abdominal cavity is opened by incising the peritoneum and the neck of the hernia lies immediately below this approach. The peritoneum is cut across posterior to the hernial orifice and the abdominal cavity is closed by suturing the anterior and posterior layers of the peritoneum. The hernial sac is then dissected out. This permits a good exposure, especially for such conditions as present a potential resection of the bowel or omentum. In the congenital hernia it is not necessary to remove the sac. Closure may be made in any one of the acceptable ways of repairing hernial defects in this region.

**Dr. E. H. Adkins**, Miami Beach, Fla., reported a case of a male, twenty-five years of age, who after lifting had a sharp pain in the abdomen. Careful study revealed preoperatively a diverticulum of the descending colon. Exploration, however, revealed a spleen which was entirely below the level of the umbilicus, the lower edge of which was in the pelvis. Splenectomy resulted in cure.

Among the high lights of the meeting were: an address by **Dr. Irvin Abell**, Louisville, Ky., characterized by symphonic eloquence and having all the profundity and high-mindedness of a prayer by Samuel Johnson, and the presidential address by **Dr. Fred Rankin**, Lexington, Ky., paying tribute to the early history of the organization and touching in an illuminating manner many of the successes on the road of surgery.

The remainder of the text is concerned primarily with a rather classic description of the various types of intestinal obstructions caused by congenital atresia, imperforate anus, obturation, Hirschsprung's disease, hernia, volvulus, intussusception, etc. Whereas this is little more than a review of the accepted facts characterizing each entity, its lucid presentation makes it a valuable addition. The text is adequately illustrated with appropriate and well-reproduced drawings and photographs. The bibliography following each section, although not very extensive, contains the more significant and pertinent references.

Whereas this monograph purposes "to set forth in a concise manner the important aspects of the therapeutic problem in obstruction of the bowel as they appear to the writer," actually it represents the recent progress and the most important contributions yet made in the management of this grave malady.

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**Collected Papers of the Mayo Clinic and Mayo Foundation, Volume XXVIII, 1936.**

Edited by Richard M. Hewitt, Lloyd G. Potter, and A. B. Nevling. Ed. 1. Cloth. Pp. 1331, with 212 illustrations. Philadelphia, 1937, W. B. Saunders Company. \$12.

Collected from many sources of publication, these papers do a real service to the reading medical public in that they not only summarize the year's productive work in the Rochester clinic but in that, in many instances, they give authoritative and up-to-the-minute information on the medical questions of the day. Covering a wide range of subjects, they offer great interest to the general practitioner and to the specialist. "What happens to gastric acidity following operations for gastric and duodenal ulcer?" "Why do some gastroenterostomies fail to function?" These and many other questions are answered in 90 articles appearing in full, in 50 by abridgment, in 80 by abstract, and in 50 by title. A few less than 300 contributors offer this material. Of unusual interest is Mann's work on "Hepatic Physiology and Pathology" and the experimental work done in his laboratory on this and other subjects.

Almost all of the subject material in this volume concerns itself with applied science as related to the practice of medicine. High lights are such subjects as, "Studies on the Influence of Certain Drugs in Relation to Biliary Pain," "The Treatment of Infections of the Urinary Tract," "Reactions Following Operation for Hyperthyroid Conditions," "Postoperative Effects of Pneumonectomy," and many others of similar nature. Dr. W. J. Mayo contributes a mellow reference to "Libraries Useful in Their Day." In short, this volume can be heartily commended to anyone interested in clinical medicine and a study of its problems. There are but few who would fail to gain considerable knowledge from its perusal.

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**Textbook of Diagnostic Roentgenology.** By Lewis J. Friedman. Pp. 623, with 638 illustrations. New York, 1937, D. Appleton-Century Co. \$10.

The need for general treatises on roentgen diagnosis is still apparent. This volume presumably fills a place between the brief texts for students and the more elaborate, detailed reference books.

With a wealth of clinical material at his disposal, the author has produced a very comprehensive survey of the subject. All phases of roentgen diagnosis are

While hermaphroditism and pseudohermaphroditism are rare conditions, they are of such importance to their victims that every physician should familiarize himself with them both so that he can recognize them and in order to familiarize himself with the possibilities of plastic surgery in enabling the patient to lead the satisfactory sexual life which the disorder usually denies him.

In addition Young discusses his experience with the "adrenogenital syndrome" in which abnormalities of the genitalia and sex characters have resulted from hyperplasia or neoplasms of the adrenal cortex and describes his operation for simultaneous exposure of both adrenals, which he advocates to obviate the disastrous results of removal of a solitary gland.

Allied conditions such as arrhenoblastoma of the ovary, hyper- and hypogenitalism, and gynecomastia are reviewed, and the relations of the various endocrine glands to the sexual organs and characteristics are reviewed. These are topics of lively interest today, and it is to be hoped that such investigations as this, coupled with those of the experimental endocrinologist, will lead at some future time to the possibility of understanding them so thoroughly that exploratory operations will become unnecessary.

The author also reviews the literature, discusses his own experience, and describes in detail the operative treatment of hypospadias, epispadias, exstrophy of the bladder, cryptorchidism, congenital valves of the prostatic urethra, and atresia ani urethralis.

This book ought to be in the hands of every urologist; the general and plastic surgeon and the internist will find much of value and even of entertainment (the case reports of pseudohermaphroditism) in it.

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**The Therapeutic Problem in Bowel Obstructions.** By Owen H. Wangensteen. Pp. 360, with 90 illustrations. Springfield, Ill., 1937, Charles C. Thomas. \$6.

Few conditions in medicine have more provokingly incited the clinical and experimental investigator than the subject of acute intestinal obstruction. That this problem thoroughly deserves such perennial inquiry and resolute research is made obvious by the lamentable knowledge that until relatively recently the mortality attending this serious condition has not been materially reduced in over a half century. However, it can be stated with gratifying encouragement that during the past decade the lights from the experimental laboratory have begun to dispel the Stygian clouds of obfuscation overhanging this grave and perplexing problem. Because no light has been more brilliant or more piercing than that of Wangensteen and his coworkers, a monograph on this subject by this investigator is eagerly received.

The author's deserving reception of the Samuel D. Gross Prize award has effected the publication of this compendium. Briefly, it is a concise elaboration of the more important aspects of the therapeutic considerations in bowel obstruction in the light of the writer's investigations and experience in this particular endeavor.

The first portion of the text is a perspicacious exposition of the physiologic effects and pathologic consequences of bowel obstruction and distention, the criteria for its early recognition, and a critical analysis of the therapeutic value of various procedures and agents. On the basis of extensive clinical and experimental investigations, the author clearly demonstrates the rational efficacy of saline solution in high obstruction (rather than low) where fluid loss is predominant, the judicious utilization of blood transfusion in strangulated obstructions, the expedient value of conservative decompression by suction applied to a duodenal tube, and the discerning indications for operation.

The remainder of the text is concerned primarily with a rather classic description of the various types of intestinal obstructions caused by congenital atresia, imperforate anus, obturation, Hirschsprung's disease, hernia, volvulus, intussusception, etc. Whereas this is little more than a review of the accepted facts characterizing each entity, its lucid presentation makes it a valuable addition. The text is adequately illustrated with appropriate and well-reproduced drawings and photographs. The bibliography following each section, although not very extensive, contains the more significant and pertinent references.

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Edited by Richard M. Hewitt, Lloyd G. Potter, and A. B. Nevling. Ed. 1. Cloth. Pp. 1331, with 212 illustrations. Philadelphia, 1937, W. B. Saunders Company. \$12.

Collected from many sources of publication, these papers do a real service to the reading medical public in that they not only summarize the year's productive work in the Rochester clinic but in that, in many instances, they give authoritative and up-to-the-minute information on the medical questions of the day. Covering a wide range of subjects, they offer great interest to the general practitioner and to the specialist. "What happens to gastric acidity following operations for gastric and duodenal ulcer?" "Why do some gastroenterostomies fail to function?" These and many other questions are answered in 90 articles appearing in full, in 50 by abridgment, in 80 by abstract, and in 50 by title. A few less than 300 contributors offer this material. Of unusual interest is Mann's work on "Hepatic Physiology and Pathology" and the experimental work done in his laboratory on this and other subjects.

Almost all of the subject material in this volume concerns itself with applied science as related to the practice of medicine. High lights are such subjects as, "Studies on the Influence of Certain Drugs in Relation to Biliary Pain," "The Treatment of Infections of the Urinary Tract," "Reactions Following Operation for Hyperthyroid Conditions," "Postoperative Effects of Pneumonecctomy," and many others of similar nature. Dr. W. J. Mayo contributes a mellow reference to "Libraries Useful in Their Day." In short, this volume can be heartily commended to anyone interested in clinical medicine and a study of its problems. There are but few who would fail to gain considerable knowledge from its perusal.

**Textbook of Diagnostic Roentgenology.** By Lewis J. Friedman. Pp. 623, with 638 illustrations. New York, 1937, D. Appleton-Century Co. \$10.

The need for general treatises on roentgen diagnosis is still apparent. This volume presumably fills a place between the brief texts for students and the more elaborate, detailed reference books.

With a wealth of clinical material at his disposal, the author has produced a very comprehensive survey of the subject. All phases of roentgen diagnosis are

While hermaphroditism and pseudohermaphroditism are rare conditions, they are of such importance to their victims that every physician should familiarize himself with them both so that he can recognize them and in order to familiarize himself with the possibilities of plastic surgery in enabling the patient to lead the satisfactory sexual life which the disorder usually denies him.

In addition Young discusses his experience with the "adrenogenital syndrome" in which abnormalities of the genitalia and sex characters have resulted from hyperplasia or neoplasms of the adrenal cortex and describes his operation for simultaneous exposure of both adrenals, which he advocates to obviate the disastrous results of removal of a solitary gland.

Allied conditions such as arrhenoblastoma of the ovary, hyper- and hypogenitalism, and gynecomastia are reviewed, and the relations of the various endocrine glands to the sexual organs and characteristics are reviewed. These are topics of lively interest today, and it is to be hoped that such investigations as this, coupled with those of the experimental endocrinologist, will lead at some future time to the possibility of understanding them so thoroughly that exploratory operations will become unnecessary.

The author also reviews the literature, discusses his own experience, and describes in detail the operative treatment of hypospadias, epispadias, exstrophy of the bladder, cryptorchidism, congenital valves of the prostatic urethra, and atresia ani urethralis.

This book ought to be in the hands of every urologist; the general and plastic surgeon and the internist will find much of value and even of entertainment (the case reports of pseudohermaphroditism) in it.

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**The Therapeutic Problem in Bowel Obstructions.** By Owen H. Wangensteen. Pp. 360, with 90 illustrations. Springfield, Ill., 1937, Charles C. Thomas. \$6.

Few conditions in medicine have more provokingly incited the clinical and experimental investigator than the subject of acute intestinal obstruction. That this problem thoroughly deserves such perennial inquiry and resolute research is made obvious by the lamentable knowledge that until relatively recently the mortality attending this serious condition has not been materially reduced in over a half century. However, it can be stated with gratifying encouragement that during the past decade the lights from the experimental laboratory have begun to dispel the Stygian clouds of obfuscation overhanging this grave and perplexing problem. Because no light has been more brilliant or more piercing than that of Wangensteen and his coworkers, a monograph on this subject by this investigator is eagerly received.

The author's deserving reception of the Samuel D. Gross Prize award has effected the publication of this compendium. Briefly, it is a concise elaboration of the more important aspects of the therapeutic considerations in bowel obstruction in the light of the writer's investigations and experience in this particular endeavor.

The first portion of the text is a perspicacious exposition of the physiologic effects and pathologic consequences of bowel obstruction and distention, the criteria for its early recognition, and a critical analysis of the therapeutic value of various procedures and agents. On the basis of extensive clinical and experimental investigations, the author clearly demonstrates the rational efficacy of saline solution in high obstruction (rather than low) where fluid loss is predominant, the judicious utilization of blood transfusion in strangulated obstructions, the expedient value of conservative decompression by suction applied to a duodenal tube, and the discerning indications for operation.

The reader will find that the book has been written for the internist, the surgeon, and the roentgenologist. It is based upon an experience with the surgical treatment of approximately 1,800 patients with pulmonary tuberculosis. The surgeon will be particularly interested in the chapters dealing with the various types of operations that may be used in obtaining collapse of the diseased lung. The indications for and the contraindications to ten such operative procedures are considered in detail. Each procedure is classified by adequate illustrations, consisting of line drawings together with serial x-rays which show the preoperative and postoperative condition of the lungs. The description of the operative technique is in most instances given in great detail. Possibly the Semb procedure and the employment of electrosurgery for the division of adhesions deserve fuller consideration. The desirable and undesirable features of each operative procedure are impartially weighed and the interrelationship of the various procedures is discussed. A consideration of the different types of tuberculous empyema is particularly instructive as is also the chapter dealing with tuberculosis of the thoracic wall.

Practically all of the book, except for the parts dealing only with operative technique, will be of interest to the internist. The choice of patients for collapse therapy and the choice of procedure for the particular patient are given careful attention. Various types of pulmonary and pleural lesions are discussed from the viewpoint of the choice of the proper treatment. The causes of failure as well as success in the care of patients are fully considered. Of particular interest to the internist are the excellent chapters by Dr. John Blair Barnwell on pneumothorax and by Dr. Kirby Smith Howlett, Jr., on oleothorax. These subjects are thoroughly and carefully considered.

The book will be of interest and help to the roentgenologist who works with and advises the surgeon and internist. The confusing shadows which may be observed after operative procedures are discussed. The findings on fluoroscopic examination before and after various forms of treatment are described.

Of interest to all will be the two excellent chapters by Dr. Max Pinner on "Physiological Principles of Collapse Therapy" and the "Pathology of Pulmonary Collapse."

The book can be recommended without reservations as an authoritative treatise of the subject.

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**Neurology.** By Roy R. Grinker, Chairman, Department of Neuropsychiatry, Michael Reese Hospital, and Professor, University of Chicago. Cloth. Pp. 999, with 406 illustrations. Springfield, Ill., 1937, Charles C. Thomas. \$8.50.

The second edition of Grinker's *Neurology* is built up along the same logical plan as the first, with emphasis well laid on the embryology, anatomy, and physiology of the various units of the nervous system as an introduction to a study of their pathology and abnormal function in disease. The anatomic figures, cross-section drawings, and photomicrographs leave little to be desired. Succeeding chapters take up the spinal fluid, the functions of the motor unit, reflex activity, and sensation on which is based the technique of neurologic examination. In a similar way careful descriptions of cerebellar function, muscle tone, the extrapyramidal motor system, and the cerebral cortex precede the more purely clinical portions of the book.

From a neurosurgical viewpoint, the chapter on intracranial tumors, written with the assistance of Dr. Percival Bailey and Dr. Paul C. Bucy and based on the extensive material to be found in the University of Chicago Clinics, is thoroughly satisfactory. The descriptions of peripheral nerve and spinal cord tumors are also good.

covered, including the physical principles, methods of technique, and dark-room procedures. There is, therefore, a considerable material between the covers of this one book.

The scope of roentgen diagnosis is so extensive that a complete presentation cannot be adequately made in so limited a space. As a result, many subjects are treated rather superficially. There is, perhaps, too much emphasis on the rarer diseases and the more bizarre roentgen manifestations. For example, bone tumors and infections are treated rather briefly while considerable space is devoted to the rare lesions, such as leprosy, osteopoikilosis, etc.

Certain features are open to specific criticism. In the fairly long chapter on fractures, nothing is stated as to methods of determining whether a proper reduction has been made. The complete separation of acute from chronic osteomyelitis seems hardly justifiable. The use of the term "tubercular" for "tuberculous" will no doubt be corrected in later editions.

The material on intestinal obstruction is open to considerable question. The author apparently prefers to give barium by mouth rather than by enema in suspected cases, advice which will not be concurred in by most surgeons and roentgenologists. The impression is created that ileocecal intussusception is rare and that only occasionally it can be diagnosed roentgenologically. Neither of these statements is sound.

While other errors of a similar nature could be pointed out, the material on the whole is sound and most of the points in dispute are not serious.

The illustrations are well selected and rather well reproduced. A bibliography is included but it is undoubtedly not intended to be complete. The book is well indexed and well printed.

The treatment accorded most of the subjects is too brief to satisfy the specialist in roentgen diagnosis. While it may have more value for other specialists, the same objection still obtains. To the general practitioner, however, this book should have considerable appeal. It enables him to obtain a brief and reasonably authoritative statement concerning almost any problem in which roentgen diagnosis is a factor. The concise and clear exposition of physics and technique will also be of value to this group. It is recommended as a valuable addition to the library of the physician practicing general medicine.

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**The Collapse Therapy of Pulmonary Tuberculosis.** By John Alexander. With 679 illustrations. Springfield, Ill., 1937, Charles C. Thomas.

When Dr. Alexander's first book, *The Surgery of Pulmonary Tuberculosis*, appeared in 1925, the surgical treatment of pulmonary tuberculosis was in its infancy throughout the world and particularly so in this country as compared to those of Central Europe. Due to a large extent to the excellence of this first book, the procedures which were discussed were rapidly adopted in America and the increase in their use has been phenomenal. A number of large sanatoria have found that some form of collapse therapy is indicated in approximately 75 per cent of their patients. The advances made during the past twelve years have more or less compelled Dr. Alexander to rewrite the entire book, except for those parts dealing with historical matters. In addition the illustrations have been almost entirely replaced and added to so that there are 367 figures that contain 679 separate illustrations. The size of the book is three or four times that of the first and the bibliography has increased from approximately 500 references to more than 1,300.

The reader will find that the book has been written for the internist, the surgeon, and the roentgenologist. It is based upon an experience with the surgical treatment of approximately 1,800 patients with pulmonary tuberculosis. The surgeon will be particularly interested in the chapters dealing with the various types of operations that may be used in obtaining collapse of the diseased lung. The indications for and the contraindications to ten such operative procedures are considered in detail. Each procedure is classified by adequate illustrations, consisting of line drawings together with serial x-rays which show the preoperative and postoperative condition of the lungs. The description of the operative technique is in most instances given in great detail. Possibly the Semb procedure and the employment of electrosurgery for the division of adhesions deserve fuller consideration. The desirable and undesirable features of each operative procedure are impartially weighed and the interrelationship of the various procedures is discussed. A consideration of the different types of tuberculous empyema is particularly instructive as is also the chapter dealing with tuberculosis of the thoracic wall.

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In the account of trigeminal neuralgia the author states that "Frazier cuts the motor root for he fears that it may bear antidromic fibers to the mesencephalic nucleus and be responsible for those rare cases of persistent pain after the sensory roots have been cut." Inasmuch as Frazier was primarily responsible for the modern operation of selective section to spare the motor root, the reason for this statement is difficult to explain. There are numerous minor inaccuracies in the chapter on the vegetative nervous system, such as statements that the pharmacologic rôle of ergotamine is to stimulate the sympathetic fibers and that the vagus constricts the gut and produces peristalsis, but relaxes the sphincters at the pylorus and cecum. The work of Cannon, Alvarez, and many others has shown that the vagus carries both stimulator and inhibitor fibers, so that no such clear-cut response will ordinarily ensue. In the section on Raynaud's disease the selection of patients suitable for operation is not adequately described, and the discussion of the best surgical method to secure relief of vasospasm seems unnecessarily vague. Furthermore, in the light of recent experimental work, the diagrams of heart and bladder innervation (Figs. 96 and 98) are inaccurate. In Fig. 96 the direct cardiac nerves, which are so important in surgical intervention of angina pectoris, are omitted, while from Fig. 98 the reader would derive the view that there is a balanced sympathetic inhibitor-parasympathetic motor tonus of the detrusor vesicae. The work of Denny-Brown, of Evans, and of Munro has clearly shown that there is no such balanced control of bladder activity. To the neurosurgeon who has treated traumatic epilepsy on the lines laid down by Penfield, the author may seem over-conservative when he states that: "I have not seen this procedure [extirpation of a cortical scar] act to stop convulsions if all sedative medication such as luminal is withdrawn."

In comparison with other textbooks of neurology, which lack the excellent introductory chapters of this volume, it must be admitted that differential diagnosis and treatment of certain diseases do not stand out with the clarity of the preliminary anatomic and physiologic sections. An additional criticism is that numerous important clinical references have been omitted. For instance, in the chapter on muscular atrophies no mention is made of the differential test for myasthenia gravis with prostigmin which was proposed in 1935 by Viets and Schwab. Mention of this omission must be made because the test is of the greatest value in ruling out such conditions as the chronic progressive ophthalmoplegia of von Graefe and bulbar poliomyelitis, with which myasthenia gravis is often confused.

Taken as a whole the text is most readable and gives a logical and clear-cut understanding of the function of the nervous system in both health and disease. The index is complete and satisfactory. In the reviewer's opinion the sound anatomic and physiologic background of the work more than outweighs the clinical shortcomings which have been pointed out above. The book is not for the specialist who requires the complete picture and the most up-to-date information on clinical neurology, but it can be recommended enthusiastically for the medical student and the general practitioner who require a single volume text on the fundamentals of neurologic disease.

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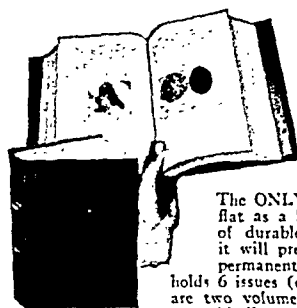
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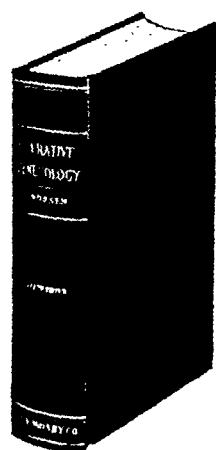
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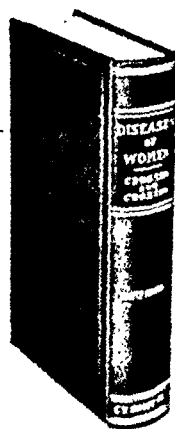
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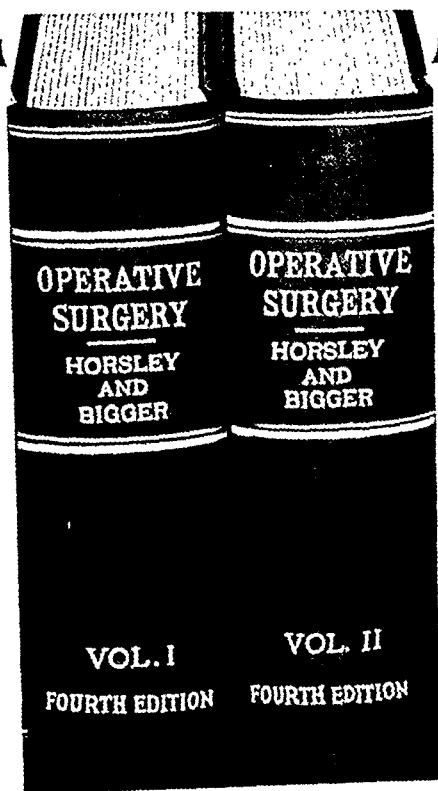
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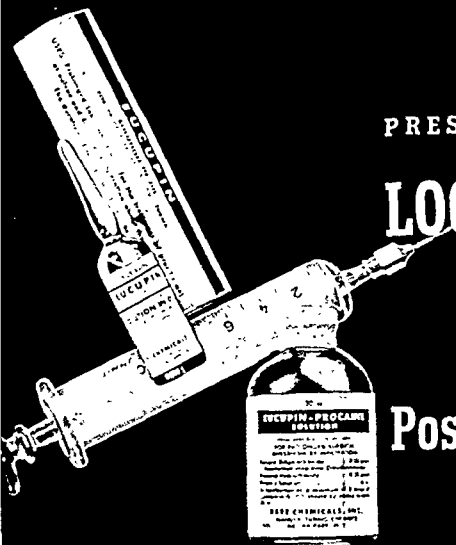
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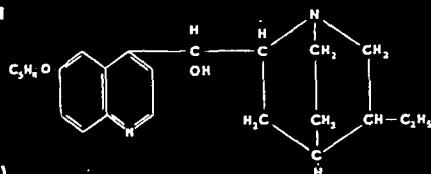
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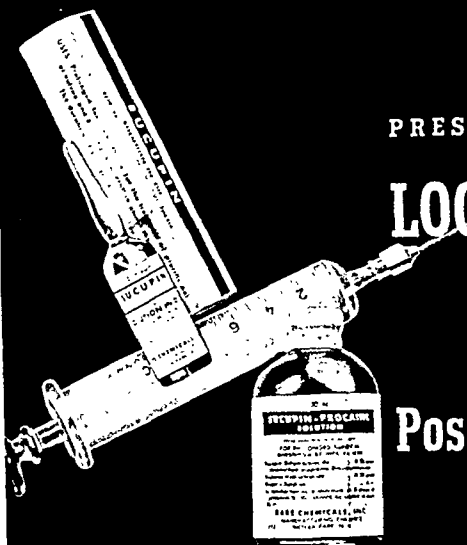
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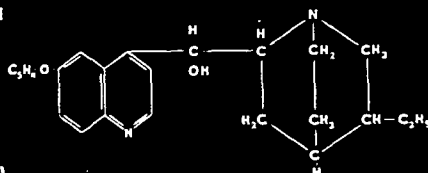
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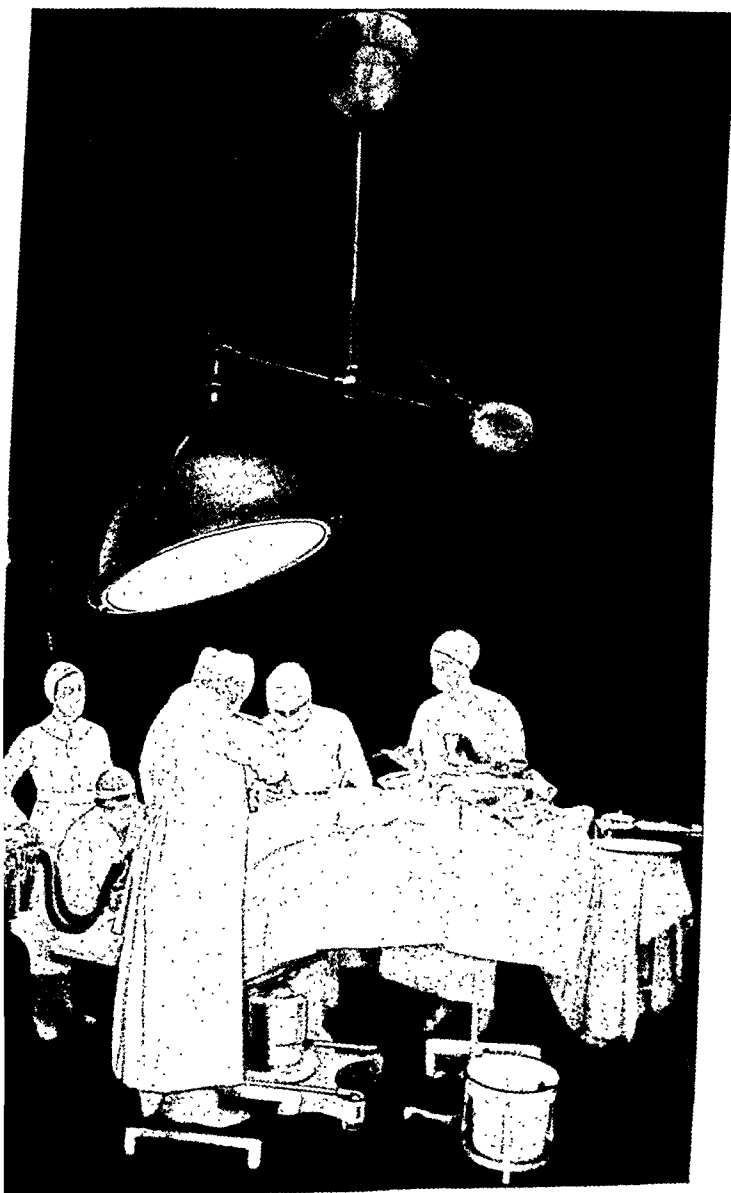
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### Original Communications

#### Symposium on Biliary Disease:

- The Effect of Recent Advances in Biliary Physiology on the Mortality Following Operation for Common Duct Obstruction.* I. S. Ravdin, M.D., J. E. Rhoads, M.D., W. D. Frazier, M.D., and A. W. Uhn, M.D., Philadelphia, Pa. ----- 805
- Applied Physiology of Liver.* L. A. Crandall, Jr., Ph.D., M.D., and A. C. Ivy, Ph.D., M.D., Chicago, Ill. ----- 815
- Noncalculous Cholecystitis.* Warren H. Cole, M.D., Chicago, Ill. ---- 821
- Röntgen Diagnosis of Surgical Diseases of the Liver and Biliary Tract.* Eugene P. Pendergrass, M.D., and George W. Chamberlin, M.D., Philadelphia, Pa. ----- 810
- The Anatomy of Gall-Bladder Incisions.* Oscar V. Batson, M.D., Philadelphia, Pa. ----- 871
- Preoperative and Postoperative Treatment in Cases of Obstructive Jaundice.* C. G. Johnston, M.D., Detroit, Mich. ----- 875
- Personal Experiences in the Treatment of Benign Obstructing Lesions of the Biliary Tract.* Wallman Walters, M.D., Rochester, Minn. 881
- Ligation and Refrigeration of Intestine.* Frederick M. Allen, M.D., New York, N. Y. ----- 803
- Experimental Attempts to Prevent or Abolish the Hypertension that is Associated With Renal Ischemia.* Sanford E. Levy, M.D., and Alfred Blacklock, M.D., Nashville, Tenn. ----- 899
- The Pathogenesis of Seminoma of the Testis.* John R. McDonald, M.D., Carl F. Schlotthauer, D.V.M., and Jesse L. Bollman, M.D., Rochester, Minn. 004

### Editorials

- Recent Advances in Our Knowledge of Biliary Function.* I. S. Ravdin, M.D., Philadelphia, Pa. ----- 912
- Continuous Drip Transfusion.* Michael DeBakey, M.D., New Orleans, La. ---- 914

### Recent Advances in Surgery

- Mammary Tumors.* Charles F. Geschickter, M.D., Baltimore, Md. ----- 916

### Review of Recent Meetings

- Review of the Thirteenth Annual Meeting of the Pacific Coast Surgical Association, Los Angeles, Calif., Feb. 22-25, 1938.* Henry H. Searls, M.D., San Francisco, Calif. ----- 930
- Report on the Meetings of the American Society for Pharmacology and Experimental Therapeutics, Baltimore, Md., March 30-April 2, 1938.* Raymond N. Bleter, M.D., St. Paul, Minn. ----- 951

### Book Reviews

- Book Reviews* ----- 937

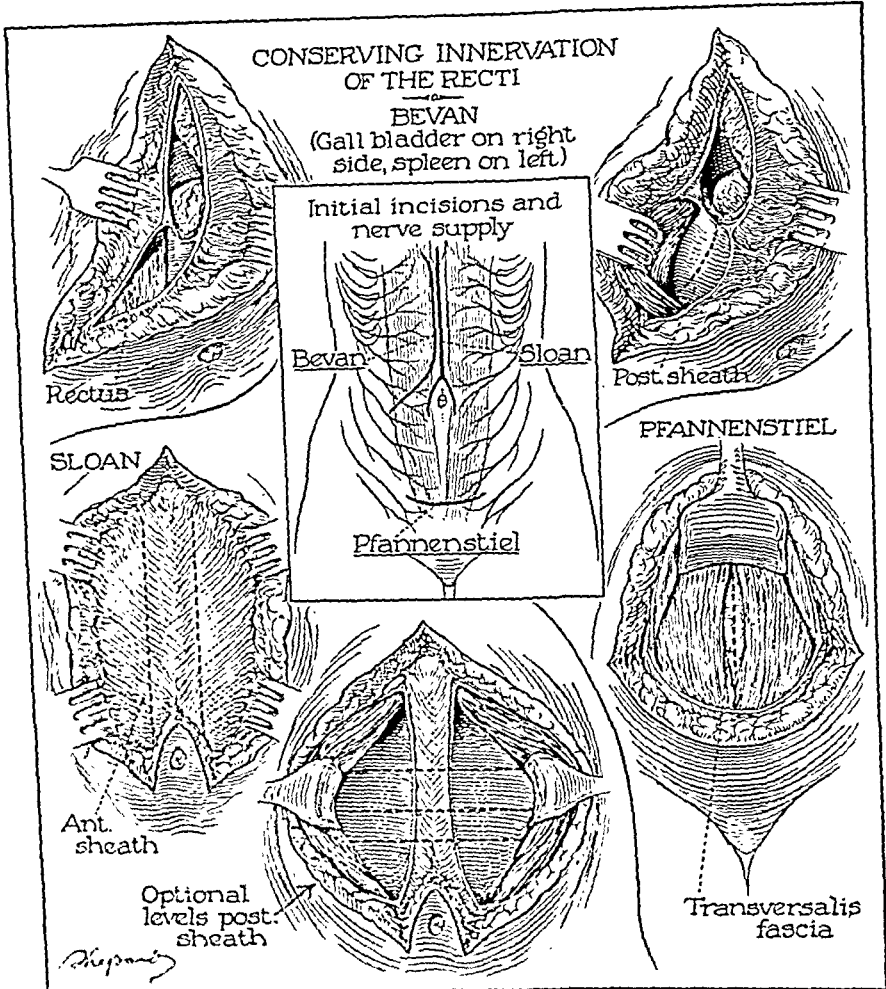
### Index

- Index* ----- 961

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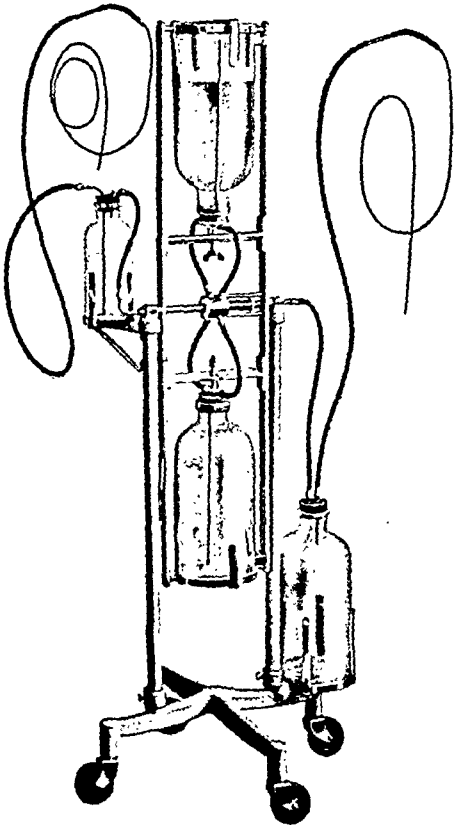
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### Partial Table of Contents

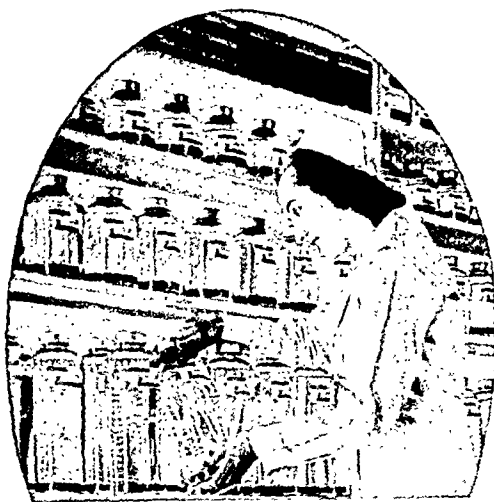
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By LEIGH F. WATSON, M.D., Member of Staff, California Lutheran and Methodist Hospitals, Los Angeles, Calif. 392 pages, 281 illustrations. PRICE, \$7.50.

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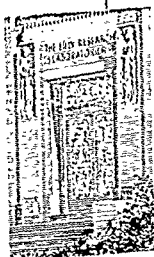
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# SURGERY

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## Original Communications

### Symposium on Biliary Disease

#### THE EFFECT OF RECENT ADVANCES IN BILIARY PHYSIOLOGY ON THE MORTALITY FOLLOWING OPERATION FOR COMMON DUCT OBSTRUCTION

I. S. RAVDIN, M.D., J. E. RHOADS, M.D., W. D. FRAZIER, M.D.,  
AND A. W. ULIN, M.D., PHILADELPHIA, PA.

*(From the Harrison Department of Surgical Research, School of Medicine, University of Pennsylvania, and the Hospital of the Surgical Clinic of the University of Pennsylvania)*

IN NO field of surgery has the physiologic approach to problems of pre- and postoperative care had greater influence than in the treatment of common duct obstruction. Largely on the basis of experimental studies special methods of treatment have been introduced. It is now time that we evaluate the effects of this treatment by an analysis of clinical results.

Between 1922 and 1937, 155 patients with obstructive jaundice were operated upon at the Hospital of the University of Pennsylvania under the observation of the senior author. It has not been possible to test each new addition to the treatment, but the series falls into three fairly equal chronological groups which afford comparison of three substantially different therapeutic regimes.

In addition to the effect on gross mortality, the effect on the incidence of those postoperative complications peculiar to jaundiced patients has been studied. Of these the most important is postoperative hemorrhage. "Pancreatic asthenia" and the so-called liver deaths have also been considered but their incidence is too low to permit statistical analysis in a series of 155 cases.

*Group I.*—The first group comprises 59 patients observed from 1922 to 1929.

These patients received small amounts of glucose by vein before operation. No consistent effort was made to raise the carbohydrate

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intake in the diet in the early years of this group, although in the final years this was done. Preoperative transfusions were not employed and after operation transfusion only rarely was resorted to unless the patient was in extremis. Biliary decompression was practically never practiced. Refeeding of bile was not practiced even when excessive quantities of bile were lost. The bilirubinemia in general was not allowed to become constant before operation. Liberal doses of calcium were routinely administered in the earlier part of this period. The usual anesthetic for operation was ether, administered by the open-drop method.

*Group II.*—The second group, consisting of 47 patients, was admitted between 1929 and 1933. The principal difference in treatment was the routine administration of glucose intravenously during both the preoperative and postoperative periods. High carbohydrate diets were ordered in addition, and it became the practice to make frequent van den Bergh determinations and to defer operation until a time when the bilirubinemia was constant. Blood transfusions were employed only occasionally in the preoperative period. In those patients who drained excessive amounts of bile, a portion of this bile was refeed by stomach tube. Occasionally a decompression apparatus was used. The use of calcium was abandoned except in rare instances. In this group spinal anesthesia and ether were used to about the same extent.

*Group III.*—The third group of 49 patients covers the period from 1933 to 1937.

Glucose solutions with and without saline were given freely by vein both before and after operation. Blood transfusions were also given routinely both before and after operation. A method for gradual decompression of the biliary tract after operation was used extensively. The practice of operating only during periods of constant bilirubinemia was continued. These differences are summarized in Table I.

TABLE I  
VARIATIONS IN PRE- AND POSTOPERATIVE THERAPY

GROUP	YEARS	NUMBER OF PATIENTS	HIGH CARBOHY- DRATE DIET	CALCIUM	SUPPLEMEN- TARY INTRA- VENOUS GLUCOSE		BLOOD TRANSFUSIONS		OPERATION DURING PERIOD OF CONSTANT BILIRUBINEMIA	BILIARY DECOMPRESSION	REFEEDING BILE
					PRE- OPERATIVE	POST- OPERATIVE	PRE- OPERATIVE	POST- OPERATIVE			
I	1922-1929	59	0	+	+	+	0	+	0	+	0
II	1929-1933	47	+	+	+	+	+	+	+	+	+
III	1933-1937	49	++	0	++	++	++	++	+	+	+

The incidence of postoperative hemorrhage, "pancreatic asthenia," and liver shock in each group and for the entire series is given in Table II.

TABLE II

INCIDENCE OF POSTOPERATIVE HEMORRHAGE, ASTHENIA, AND LIVER SHOCK

GROUP	POSTOPERATIVE HEMORRHAGE (PER CENT)	PANCREATIC ASTHENIA (PER CENT)	LIVER SHOCK (PER CENT)
I	22.0	2.0	2.0
II	19.1	2.0	4.2
III	18.4	0.0	0.0
Entire series	20.0	1.3	2.0

It appears that "pancreatic asthenia" and liver shock have been encountered with decreasing frequency. Postoperative hemorrhage, however, remains a common complication of operations upon jaundiced patients, but it has been possible to reduce the degree of the bleeding and the mortality of the complication. This is shown in Table III.

TABLE III

THE RELATION OF POSTOPERATIVE HEMORRHAGE TO MORTALITY

GROUP	NUMBER OF PATIENTS	NUMBER WITH POSTOPERA- TIVE BLEEDING	PATIENTS DYING PRIMARILY OF HEMOR- RHAGE	HEMOR- RHAGE MORTALITY (PER CENT)	FATAL CASES IN WHICH HEMOR- RHAGE OCCURRED	GROSS MORTALITY OF PATIENTS WITH POST- OPERATIVE HEMOR- RHAGE (PER CENT)
I	59	13	5	8.5	9	69.0
II	47	9	2	4.2	3	33.0
III	49	9	1	2.0	2	22.0

An analysis of the causes of death in the three groups is summarized in Table IV. The deaths recorded in the last column of Table IV were due to pneumonia, wound rupture, malignancy, cerebral thrombosis, peritonitis, and other conditions encountered in many types of surgical patients.

Before crediting the various therapeutic measures outlined with the improvement in mortality, it is necessary to compare the three groups in respect to age, duration of jaundice, and the type of anesthesia

TABLE IV

ANALYSIS OF DEATHS

GROUP	MORTALITY ENTIRE GROUP (PER CENT)	MORTALITY DUE TO HEMOR- RHAGE (PER CENT)	MORTALITY DUE TO PANCREATIC ASTHENIA (PER CENT)	MORTALITY DUE TO LIVER SHOCK (PER CENT)	MORTALITY DUE TO COMPLICA- TIONS PECULIAR TO JAUNDICED PATIENTS (PER CENT)	MORTALITY DUE TO OTHER CAUSES (PER CENT)
I	22.0	8.5	1.7	1.7	11.9	10.1
II	12.7	4.2	1.7	4.2	10.1	2.6
III	8.6	2.0	0.0	0.0	2.0	6.6

used. Unfortunately the data were not available in every case. Table V shows these comparisons for those cases in which the necessary information was on record.

TABLE V

GROUP	MEAN AGE	DURATION OF JAUNDICE			ANESTHESIA	
		1 TO 14 DAYS (PER CENT)	15 TO 60 DAYS (PER CENT)	OVER 60 DAYS (PER CENT)	ETHER (PER CENT)	SPINAL (PER CENT)
I	51.4	49.0	29.0	22.0	63.0	17.0
II	49.8	58.5	37.5	4.0	45.0	59.0*
III	49.9	42.5	39.4	18.1	12.0	82.0

\*Some patients had ether and spinal anesthesia. The occasional use of nitrous oxide and oxygen or local anesthesia is not tabulated.

## DISCUSSION

The surgery of any vital organ necessarily presents special problems related to impaired or suspended function of that organ. This is peculiarly true of surgery of the liver where one deals with an unpaired organ many of the functions of which are even now not clearly understood. There is no general agreement among physiologists on many of the functional activities of the liver and much less agreement on how others of these are accomplished. In addition, the liver has so great a functional reserve that there are no means now available of accurately discovering the extent of early stages of liver damage. None of the suggested tests of liver function gives definite significant information until the liver damage has progressed to a considerable degree. One of the most important sequelae of long standing cholecystitis and common duct obstruction is damage to the liver parenchyma. The chief mechanisms by which the damage is brought about are infection, interference with blood supply with resultant anoxemia, and the effects of pressure on the hepatic cells.

In obstructive jaundice, due to stone, there is frequently, if not always, some infection. This is evidenced by the chills and fever so regularly seen in the intermittent common duct obstruction described by Charcot.<sup>2</sup> The evaluation of the rôle which pathogenic organisms, commonly found in the bile, may play in liver injury needs further investigation. The flora of the biliary tract may vary, but except in suppurative cholangitis they rarely seem virulent enough to cause extensive injury unless associated with obstruction of the common bile duct or long standing cholecystitis.

The secretory power of the liver cells is sufficient to secrete bile against a pressure obstacle of as high as 270 mm. of bile. Between 280 and 330 mm. of bile pressure the secretion of bile ceases. It is probable that the distention of the intrahepatic bile ducts by pressure alone results in injury of the periductal parenchymal cells since the

liver is not capable of rapid distention. Varying degrees of obstruction to blood flow result and the anoxemia thus produced contributes still further to liver injury.<sup>19</sup> The observations of Levy and Blalock<sup>11</sup> that common duct obstruction is associated with an increased portal venous blood flow are at variance with the many observations we have made showing portal venous congestion and an increased portal venous pressure during complete ductal occlusion. The rupture of biliary capillaries may lead to areas of necrosis. The circulation may adjust itself by an increase in the portal venous pressure, but when the ductal occlusion is suddenly released massive hyperemia and extravasation may result as demonstrated by Ravdin and Frazier<sup>16</sup> and by Klopp and Cantarow.<sup>10</sup>

Over twenty years ago Opie and Alford<sup>13</sup> called attention to the protection which a high carbohydrate diet afforded the liver against the necrotizing effects of chloroform. Since that time it has been supposed that the presence of an adequate liver glycogen protected the liver against the injury imposed by volatile anesthetics. In work soon to be reported from this department it will be demonstrated that a greatly increased glycogen level does not protect the liver against injury if there is simultaneously present a high level of the liver fat. Although in general the Rosenfeld<sup>20</sup> hypothesis of a reciprocal relationship between liver glycogen and liver fat may be maintained, we have encountered so many exceptions to this generalization that it is not safe to conclude that a high liver glycogen concentration necessarily indicates a low liver fat concentration. Furthermore, should chronic liver injury result in an increased content of liver fat, it may be more difficult to displace the fat by the simple administration of carbohydrates. Goldschmidt, Vars, and Ravdin<sup>6</sup> have stated that the amount of fat present in the liver is the most important factor in conditioning necrosis following the administration of fat soluble anesthetics and that the protective rôle of the carbohydrate depends upon displacement of the liver fat during the deposition of liver glycogen.

It is less easy to explain why glucose decreases the clotting time in obstructive jaundice<sup>17</sup> and why, even though it may not affect bleeding or clotting time, it seems to reduce hemorrhage mortality. Clinicians are agreed, however, that the patient with a damaged liver fares better on a high carbohydrate intake. It is generally agreed that the main object of carbohydrate therapy is to produce a high glycogen level in the liver, but it is not so generally understood by clinicians that the success of this therapy depends in large part upon the simultaneous displacement of liver fat. It is often difficult to do this in the presence of common duct obstruction as evidenced by sections of the liver from some of the patients in Group III of this series (Fig. 1).

In 1929 Ravdin<sup>15</sup> recommended that intravenous infusions of glucose be used to supplement a high carbohydrate diet in the preopera-



tive period. Experiments, soon to be reported, have shown that in the dog it is possible with large intravenous glucose infusions and strenuous oral administration of carbohydrates to produce a high liver glycogen in dogs whose common ducts have been obstructed. Admittedly this form of obstruction is often not comparable to the clinical types where even more intensive therapy is necessary.

Of all the problems peculiar to the surgery of jaundice, none has received more attention than the tendency to hemorrhage. This tendency may be so marked that spontaneous bleeding may occur from the mucous membranes. Usually, however, it occurs from the operative site, sometimes from the wound, sometimes from the bile passages, and sometimes from both.



Fig. 1.—Photomicrograph of autopsy specimen of liver from a patient with long-standing common duct obstruction after thorough pre- and postoperative treatment with carbohydrates.

Many authors have regarded this bleeding tendency as due to a deficiency of some of the normal constituents required for the clotting process. Gunther and Greenberg<sup>7</sup> have shown that neither the ionized nor nonionized calcium is deficient in the blood of patients with common duct obstruction unless there is an associated serum protein deficiency, when only the nonionized calcium level is disturbed.

It is not improbable that in children, as in young dogs, a low calcium level frequently accompanies jaundice and it is true that the serum calcium is frequently lowered in the presence of hypoproteinemia; but the serum protein is markedly low in only the exceptional adult patient with obstructive jaundice. We do not feel that the experimental data or our clinical experience justifies the preoperative use of calcium and we have abandoned its use since 1932 except in children and in the presence of hypoproteinemia.

The recent investigations of Nygaard<sup>12</sup> and Quick and others<sup>14</sup> indicate a deficiency of prothrombin in the blood of the jaundiced patient, but Eagle<sup>4</sup> has not been able to demonstrate a prothrombin deficiency in the blood of animals with obstructive jaundice. The recent suggestion that vitamin K may be deficient in these patients is of considerable interest.

Not only has the cause of the hemorrhagic tendency remained obscure but innumerable attempts to determine preoperatively which patients will and which will not bleed have been in the main unsuccessful.

Several general considerations are believed to influence the hemorrhagic tendency. Thus, it is believed that the duration of the jaundice is a factor in producing the hemorrhagic tendency. The data compiled from this series of cases lend some support to this belief (Fig. 2).

As in all other hemorrhagic diatheses, recourse is ultimately had to transfusion. In the third period of our clinical study, transfusion has

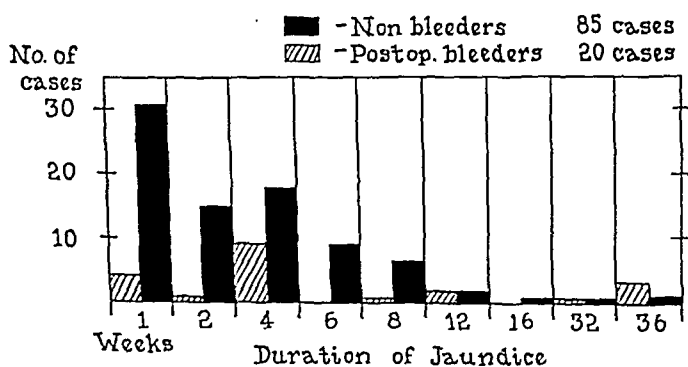


Fig. 2.—The relation of the duration of jaundice to the incidence of postoperative hemorrhage.

been used prophylactically. The fact that the incidence of hemorrhage has not declined would seem to throw serious doubt on the advantage of preoperative transfusion without other indications, such as anemia. However, we believe that, although the hemorrhage incidence has remained the same, the degree of hemorrhage has been markedly reduced, and that we have been less alarmed by the extent of the bleeding. In fact, we have recorded some instances of postoperative bleeding that might have been disregarded by some observers.

The occasional occurrence of hypoproteinemia in patients with biliary tract disease and the frequent association of hypoproteinemia with delayed wound healing<sup>21</sup> we believe would especially indicate transfusion before operation. No doubt serum transfusion would serve as well for this purpose as whole blood.

Progressing from the preoperative measures based on scientific experiments toward those based solely on clinical experience, one comes finally to the selection of the time for operation with respect to the

level of the van den Bergh test. It has long been customary to postpone operation in the face of decreasing jaundice as long as the serum bilirubin continues to fall. It has been found wiser, however, similarly to postpone operation, if the jaundice is increasing, until a constant bilirubin level has been reached (Walters<sup>22</sup>).

The anesthetic agent used for operation undoubtedly has a very important bearing on the patient's recovery. Obviously the known anesthetics causing liver injury, chloroform, avertin, and divinyl ether are contraindicated. As prolonged diethyl ether anesthesia, especially when associated with anoxemia, is capable of producing similar liver injury,<sup>5</sup> we believe that it is to be avoided when possible.

The studies of Rich<sup>19</sup> and Goldschmidt, Ravdin, and Lucke<sup>5</sup> indicate that the liver cells are exceedingly sensitive to a reduced oxygen tension. If this be true, the use of any gas mixtures, which do not provide ample oxygen in the blood, is likely to be harmful. We have no evidence that cyclopropane is harmful though, like local anesthesia, it is unlikely to permit sufficient relaxation for adequate exposure.

The anesthetic of choice, we believe, is spinal anesthesia. The chief drawback, that of a drop in blood pressure with reduction in blood flow through the liver and resultant liver anoxemia, may be overcome in most cases by the use of ephedrine preoperatively.

During the postoperative period, the problem of liver insufficiency may persist in even greater degree because of trauma and anesthesia and treatment during this period must be designed to meet this. The glucose intake must be kept up and as the patient seldom takes much by mouth during the initial phase of the postoperative period a continuous venoclysis of a glucose solution should be given. A high carbohydrate diet should be given as soon as possible.

The problem of keeping up the oxygen supply of the liver parenchyma presents several important aspects. It is of prime importance in this regard to maintain the respiratory exchange and to prevent atelectasis or other pulmonary complications. To this end it is the rule to insist on hourly change in position and hourly deep breathing exercises reenforced, if cooperation is not forthcoming, by inhalations of oxygen (90 per cent) and carbon dioxid (10 per cent). Any tendency for mucus to collect in the bronchial tree is combatted with expectorants, steam inhalations, and regular encouragement of the patient to cough. To reduce incisional pain during coughing, a tight binder is applied and often an attendant supports the patient's abdomen with his hands during the attempts to cough up the mucus. Atropine is not employed as we believe it makes the bronchial secretions thicker and more likely to occlude the bronchi.

A transverse or subcostal incision is used routinely which seems to permit abdominal respiration sooner than the right rectus incisions. On the basis of the statistics collected by Ravdin and Kern,<sup>18</sup> every reasonable endeavor is made to complete the operation in as short a

time as possible. In occasional instances patients have been given oxygen therapy after operation with the hope that higher oxygen tension would lead to better oxygenation of the liver cells.

Anemia should be corrected preoperatively and if much blood loss is sustained at operation, it should be promptly repaid by transfusion. It is of particular importance to prevent any depletion of blood volume as the resultant circulatory adjustment may seriously lower the arterial oxygen tension and blood flow to the liver may be seriously reduced.

The importance of biliary decompression has already been referred to and is discussed fully by Ravdin and Frazier.<sup>16</sup> While admitting the theoretical advantages of clamping the common duct before it is opened as recommended by Culligan,<sup>3</sup> the practical disadvantages of this maneuver have yet to be overcome. After the tube is sutured into the common duct, decompression should be carried out by a continuous method rather than by the intermittent method of Culligan.

The incidence of "pancreatic asthenia" became extremely low with the introduction of the practice of refeeding bile to patients with prolonged excessive bile drainage. By increasing the pressure in the drainage tract with a decompression apparatus, the excess bile can usually be forced into the duodenum, thus obviating the cumbersome method of refeeding bile through a stomach tube.

"Liver shock," like "pancreatic asthenia," has become a rare complication. As a condition similar to "liver shock" regularly appears in dogs when the hepatic artery is ligated, it seems possible that this condition is related to liver anoxemia. It would seem possible that an occasional instance of human liver shock might be due to unintentional ligation of an hepatic artery or to thrombosis of this vessel during convalescence. This condition is included by Heyd<sup>8</sup> and by Boyce and McPettridge<sup>1</sup> in their discussions of so-called liver death. It is nearly always encountered in the group of patients who die within forty-eight hours with high fever.

These authors describe a second symptom-complex, the hepatorenal syndrome, which they consider a later phase of the same process. This is characterized by increasing oliguria leading to anuria and terminal uremia, ten to fourteen days after operation. Only one patient in this series died in uremia. No autopsy was obtained, and it has been impossible to determine whether this case belongs in this group.

The largest single factor in the operative mortality of jaundiced patients was hemorrhage. This occurred in about 20 per cent of the patients in each of the three groups but resulted fatally in a decreasing percentage in the later groups. The treatment of hemorrhage has been transfusion. In one case twenty-two transfusions were given before a favorable outcome was achieved. Locally attempts have been made to check the hemorrhage with stryphnon gauze packs, but packing usually accomplishes little. When hemorrhage from the ducts persists

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Anemia should be corrected preoperatively and if much blood loss is sustained at operation, it should be promptly repaid by transfusion. It is of particular importance to prevent any depletion of blood volume as the resultant circulatory adjustment may seriously lower the arterial oxygen tension and blood flow to the liver may be seriously reduced.

The importance of biliary decompression has already been referred to and is discussed fully by Ravdin and Frazier.<sup>16</sup> While admitting the theoretical advantages of clamping the common duct before it is opened as recommended by Culligan,<sup>3</sup> the practical disadvantages of this maneuver have yet to be overcome. After the tube is sutured into the common duct, decompression should be carried out by a continuous method rather than by the intermittent method of Culligan.

The incidence of "pancreatic asthenia" became extremely low with the introduction of the practice of refeeding bile to patients with prolonged excessive bile drainage. By increasing the pressure in the drainage tract with a decompression apparatus, the excess bile can usually be forced into the duodenum, thus obviating the cumbersome method of refeeding bile through a stomach tube.

"Liver shock," like "pancreatic asthenia," has become a rare complication. As a condition similar to "liver shock" regularly appears in dogs when the hepatic artery is ligated, it seems possible that this condition is related to liver anoxemia. It would seem possible that an occasional instance of human liver shock might be due to unintentional ligation of an hepatic artery or to thrombosis of this vessel during convalescence. This condition is included by Heyd<sup>8</sup> and by Boyce and McFetridge<sup>1</sup> in their discussions of so-called liver death. It is nearly always encountered in the group of patients who die within forty-eight hours with high fever.

These authors describe a second symptom-complex, the hepatorenal syndrome, which they consider a later phase of the same process. This is characterized by increasing oliguria leading to anuria and terminal uremia, ten to fourteen days after operation. Only one patient in this series died in uremia. No autopsy was obtained, and it has been impossible to determine whether this case belongs in this group.

The largest single factor in the operative mortality of jaundiced patients was hemorrhage. This occurred in about 20 per cent of the patients in each of the three groups but resulted fatally in a decreasing percentage in the later groups. The treatment of hemorrhage has been transfusion. In one case twenty-two transfusions were given before a favorable outcome was achieved. Locally attempts have been made to check the hemorrhage with strychnon gauze packs, but packing usually accomplishes little. When hemorrhage from the ducts persists

for several days, it may be wise to remove all the drainage tubes, including the tube from the common duct.

After the release of common duct obstruction, several weeks may pass before the liver bile shows evidence that hepatic function has returned to normal. A high carbohydrate intake should be maintained not merely until jaundice has disappeared but until bile salts have reappeared in good concentration and the cholesterol concentration returns to normal in the bile. Except in the face of persistent hemorrhage over a considerable period, the common duct tube should not be removed until these changes can be demonstrated. It is also routine to inject the tube with lipiodol for x-ray visualization of the common duct before its removal.

The lag period between the release of obstruction and the recovery of liver function cannot be too strongly emphasized. Judd, Snell, and Hoerner<sup>9</sup> have reported bleeding in patients in whom jaundice was no longer present but in whom liver injury remained. A similar case was observed in the Hospital of the University of Pennsylvania in 1936.

#### CONCLUSIONS

1. A group of 155 patients operated on for obstructive jaundice has been analyzed for the effect of a changing pre- and postoperative regime on morbidity and mortality.

2. The operative mortality has been greatly reduced.

3. The incidence of postoperative hemorrhage has not been influenced by changes in our preoperative preparation; but the degree and extent of the hemorrhage have been influenced and the mortality from postoperative hemorrhage has been markedly reduced.

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## APPLIED PHYSIOLOGY OF LIVER

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TO APPRECIATE the advances made within the last three decades in our knowledge of the functions of the liver, one need only turn to the first essentially modern textbook of physiology (Schafer, 1898). The general principles of carbohydrate and protein metabolism had been laid down, but little was known of the metabolism of fat in this organ, of the secretion of bile aside from the general chemical constitution of this fluid, or of the many other functions of the liver. Little of the information available was capable of clinical application. Since the turn of the century, details have been supplied in those fields where only broad generalizations had been available, and many facts directly applicable to medical practice have been discovered. As is the case in all branches of science, discoveries that possess great practical significance may be in themselves but minor details of the general picture, and are often entirely dependent upon an immense amount of previous experiment and observation which has but little immediate applicability.

Notwithstanding the advances that have been made, the functions of the liver remain one of the least developed frontiers of medicine. When the liver is removed surgically, death ensues within about twelve hours unless glucose be given to maintain the blood sugar level. But even though the normal blood glucose range be maintained, death cannot be postponed more than twenty-four to thirty-six hours at the most. The cause of the fatal termination which then occurs is unknown. And it is significant that this is true of no other organ in the body; in every other instance either the cause of death is known or replacement therapy is effective. Contributions dealing with new aspects of hepatic activity are frequent; for example, only within the last few years has it become apparent that the liver is primarily concerned with the metabolism of oxalic and citric acids. Although such accretions to our information may not be immediately applicable, they serve to fill in the picture which, as it grows more and more complete, will increasingly permit the treatment of hepatic disease to be placed on a sound and logical basis.

As new facts are discovered, there is a tendency to attempt an immediate application for the purpose of testing liver function. The

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obstacles facing a "liver function test" have often been emphasized. The large factor of safety, some 80 per cent of the organ being removable without apparent change; the diversity of functions, giving no assurance that impairment of one function means deficient activity of the organ as a whole; the difficulties of experimental investigation and especially of clinical study; all these complicate a study of the functions of the liver and even more seriously disturb an evaluation of the state of those functions by arbitrary tests. A discussion of the liver is most conveniently divided according to the various types of metabolic activity with which this organ is concerned. Since it is questionable whether any of our present tests of liver function are satisfactory, these are best included in the discussions of those functions which they purport to evaluate.

#### THE SECRETION OF BILE

Since cholecystitis and cholelithiasis are more common than any other biliary tract disease and are apparently far more common than all affections of the liver itself, the gall bladder has attracted more clinical interest than any other part of the liver and biliary tract system. Ray<sup>1</sup> has recently analyzed a large number of human gallstones and finds no essential difference in chemical constitution between those that have been referred to as calcium-cholesterol-pigment stones and those called cholesterol-pigment stones. Stones from the same gall bladder were always very similar and even stones of different appearance and of presumably different types did not vary in any consistent or striking manner. Riegel and others<sup>2</sup> have since found calcium to vary from traces to 28 per cent, while the cholesterol values given are usually above 70 per cent. Even such variations do not necessarily bespeak multiple causes for calculus formation, while Ray's conclusions are compatible with the concept that a single factor may be the primary cause. Walsh and Ivy<sup>3</sup> have discussed the various theories that have been proposed and have come to the conclusion, which must be that of any impartial observer, that at present no definite decision can be reached concerning the relative importance of pH, stagnation, decreased concentration of bile salts, and other possible factors in human cholelithiasis.

A consistent and striking observation is the decreased concentration of bile salts found when stones are present in the gall bladder or when the gall bladder is damaged.<sup>4-7</sup> Since the bile salts are essential for the solution of all the lipids in bile, including cholesterol, the demonstration of a decrease in bile salt concentration is strongly suggestive of a direct relationship of this change to stone formation. It should be noted also that both bile salt and cholesterol concentration have been found by Riegel, Ravdin, and Rose<sup>8</sup> to be decreased in the biliary

drainage of patients with liver damage; the decrease in bile salt concentration was proportionately greater than that of cholesterol. Bollman and Mann<sup>9</sup> have produced evidence that the liver is the sole site of bile salt formation, that it plays the major rôle in the destruction of bile salts, and that liver poisons, such as chloroform, carbon tetrachloride, or tetrachlorethylene, can produce such a marked decrease in bile salt formation that only traces are present in the bile. If one considers the tempting hypothesis that the mechanism of stone formation is a precipitation of fatty acids and cholesterol secondary to a decrease in bile salt concentration, then it appears that this decrease may occur either as a result of impairment of liver function or because of increased absorption of bile salts through the wall of a damaged gall bladder.<sup>2, 7</sup>

An important consideration arising from the demonstration that the production of bile salts may be so greatly decreased by liver damage is the questionable value of returning such bile to the gastrointestinal tract as is the usual practice in cases of biliary fistula. The value of bile for the digestive tract, according to all information, lies in its bile salt content. It would seem far more beneficial to administer bile salts by mouth in the maximum dosage tolerated than to return drainage bile in which the bile salt concentration may be negligible.

It should be noted that Golber<sup>10</sup> has observed an increase in cholesterol and a decrease in bile salt in the bile in thyrotoxicosis, and discusses the bearing on gallstone formation. Riegel and others<sup>11</sup> have removed specimens of gall bladder bile from living pregnant women at term and found an increased cholesterol and decreased bile salt content; this suggested to them both a change in the character of the liver bile and a decrease in the absorptive ability of the gall bladder. Hawkins and Whipple,<sup>12</sup> in a recent review of their investigation on dogs with biliary fistulae, note that cholelithiasis may occur in such animals if they are not given bile by mouth. This might be attributed to a decrease in bile salt concentration as a result of long continued drainage.

The presence of bile in the intestine aids in the hydrolysis of fats by lipase and is essential for normal absorption of the fatty acids. Greaves and Schmidt,<sup>13</sup> confirmed by Taylor, Weld, and Sykes,<sup>14</sup> have shown that bile (bile salts) is essential for the absorption of vitamin D. Later Greaves and Schmidt<sup>15</sup> showed that while vitamin A can be absorbed from the intestine in the absence of bile, carotene (the precursor of vitamin A) cannot. Exclusion of bile from the intestine therefore may be expected to result in decreased fat absorption and possible vitamin A and D deficiencies. Hawkins and Whipple<sup>12</sup> have shown that in biliary fistula dogs one may find not only the cholelithiasis mentioned above but also purpura, possibly due to lack of prothrombin,

osteoporosis which may be secondary to a vitamin D deficiency, duodenal ulcers, and intestinal intoxication. Liver feeding much improved the general condition of their animals. While such disturbances as these may be anticipated in patients with bile fistulae, the more common condition of jaundice with partial or complete exclusion of bile from the intestine is an even more complex syndrome. Ivy<sup>16</sup> has reviewed the disturbances incident to jaundice. Quick and others<sup>17</sup> have since found the prothrombin content of the blood decreased in this condition, which may serve to explain the increased tendency to hemorrhage, the reason for which has not previously been clear.

The most serious aspect of jaundice, and that responsible for much of its symptomatology, is the associated disturbance of liver function which obviously is primary in toxic or infectious jaundice and is inevitable as a secondary result of an obstructive jaundice which persists for any length of time. It would seem that the surgeon assumes a considerable risk in operating upon a patient with known hepatic pathology or with biliary tract disease of such long standing that liver function may be presumed to be impaired.

Quick<sup>18</sup> has found his hippuric acid excretion test for liver function negative in obstructive jaundice of short duration, as it usually is in cholecystitis and cholelithiasis, but as complete obstruction persists there are pathologic changes in the liver, increasingly severe functional impairment of that organ, and eventual death. Cantarow and Stewart<sup>19</sup> state that the intravenous administration of sodium dehydrocholate to cats with ligated common bile ducts decreased the regressive lesions in the liver, produced persistence of the stainable lipids, and aided in maintaining the serum bilirubin.

#### CARBOHYDRATE METABOLISM

Clinically, the most important aspects of hepatic carbohydrate metabolism are (1) the importance of the liver for the regulation of the blood sugar level, so that in any instance of hypoglycemia it is necessary to consider whether it may not be of hepatic origin; and (2) the importance of an adequate glycogen store for the maintenance of normal liver function and the value of promoting glycogen deposition in the management of hepatic disease.

The hypoglycemiae that accompany adrenal and pituitary insufficiency in all probability are due to failure of the liver to liberate glucose into the blood at the normal rate. Crandall and Cherry<sup>20</sup> have shown that after hypophysectomy the amount of glucose added to the blood by the liver is less than normal and that in hypophysectomized or adrenalectomized animals the liver does not respond to insulin hypoglycemia in a normal manner by the liberation of increased amounts of glucose. In the normal animal hypoglycemia causes an

increase in the production of glucose by the liver; this is not true in adrenal or pituitary insufficiency. Thus, it is clear that the liver is the primary factor in the regulation of the normal blood sugar level; that is, it is the major factor in the homeostasis of the blood glucose.

When glucose is absorbed from the intestine, the liver carries on its homeostatic activity by stopping the formation of glucose and by removing a considerable amount of this sugar from the portal blood.<sup>21</sup> In this way an excessive hyperglycemia after glucose ingestion is prevented. In spite of these known activities function tests based on glucose administration have been of little value; too many other factors enter into blood sugar regulation.

The importance of gluconeogenesis (the conversion of nonsugars, such as lactic acid, amino acids, glycerol, etc., into glycogen or glucose) for the maintenance of the glucose supply of the body is illustrated by the decrease in glycosuria which occurs when diabetics develop cirrhosis of the liver.<sup>22</sup> In confirmation of such clinical observation it has been shown that experimental liver injury reduces glycosuria in the depancreatized dog,<sup>23</sup> while hepatectomy causes an abrupt fall in blood sugar in the diabetic animal.<sup>24</sup> It is probably a failure of gluconeogenesis which is responsible for the decreased glycosuria after hypophysectomy or adrenalectomy in experimental diabetes.<sup>25</sup> Patients with hepatic disease require increased amounts of sugars in the diet, best given in the form of glucose, not only to promote the storage of glycogen but also to meet the normal glucose requirement of the body since the liver becomes incapable of a normal production of this sugar from noncarbohydrate sources. In view of the diminished glycogen storage capacity present in liver disease, the administration of glucose should be as nearly continuous as possible in severe cases. But there would seem to be no need of intravenous injection unless the oral route is impractical.

In recent years the importance of producing maximal glycogen deposition in the presence of hepatic disease has been emphasized. A high glycogen content seems to improve the ability of the liver to carry out its various functions, and high carbohydrate diets have become accepted therapy. Both Ravdin<sup>26</sup> and Stone<sup>27</sup> have shown that liver regeneration is most rapid on those diets which permit the greatest deposition of glycogen. Stone has also observed that on starvation the liver glycogen fell most abruptly and to the lowest levels in those animals that had been receiving high carbohydrate diets. This illustrates the importance of constantly maintaining a high carbohydrate intake in the presence of severe hepatic pathology. Jones<sup>28</sup> has emphasized the marked improvement in the results obtained in the treatment of various types of hepatic disease since the introduction of intensive glucose therapy.

Many of the substances which are used by the liver for gluconeogenesis, such as amino acids and lactic acid, as well as other sugars (levulose and galactose) which are converted into glucose by the liver, have been used in testing liver function. In general it may be said that hepatic activity must be much impaired before positive results are obtained. While such tests fail to detect early and slight hepatic involvement, the use of galactose or levulose may aid in differentiating infectious from obstructive jaundice, since they are not positive in the latter unless pathologic changes have occurred secondary to long continued obstruction.

#### LIPID METABOLISM

It is not yet known whether the liver is essential in the metabolism of fats, but there is no question that it plays an important rôle. A striking fact that seems to have been insufficiently emphasized is the change in fat deposition in human liver disease and experimental liver injury. A loss of fat from the subcutaneous tissues, giving a loss of skin turgor and a wasted appearance that may be mistaken for dehydration, is often seen in those cases of cirrhosis where hepatic function seems to be gravely disturbed. A similar loss of subcutaneous and depot fat in Eck fistula dogs is mentioned by Crandall and Anderson,<sup>29</sup> who showed that the appearance of these animals is not due to dehydration. Crandall and Ivy<sup>30</sup> have briefly discussed the low blood lipid level of Eck fistula animals and the decreased response to oral fat administration. The loss of depot fat, however, remains unexplained.

It is well known that extensive deposition of liver fat may occur after the administration of hepatotoxins such as chloroform, or in the absence of the external secretion of the pancreas, and it has been shown also by the extensive studies of Best and his collaborators to develop when the choline and betaine content of the diet is minimal. Choline or betaine prevents the abnormal accumulation of liver fat that otherwise occurs after pancreatectomy in experimental animals; it also can prevent the deposition of fat on high fat or high cholesterol diets.<sup>31, 32</sup> Since extensive fat accumulation in the liver depresses hepatic function, choline or betaine may be found clinically useful, especially in cases where liver lipid deposits are believed to have resulted from pancreatic fibrosis with lack of external pancreatic secretion. More recently Dragstedt, Prohaska, and Harms<sup>33</sup> have found a substance, apparently not a choline derivative, in defatted alcoholic extracts of pancreas which prevents the development of fatty livers in depancreatized dogs; they suggest that this substance may be a hormone and have termed it "lipocaine."

It seems well established that the liver is the site of ketone body formation. It is not surprising, therefore, that hypophysectomy should

diminish or abolish ketone body excretion, as it does the glycosuria, in experimental diabetes.<sup>34</sup> On this basis an attempt has been made to treat human diabetes by subjecting the pituitary gland to deep x-ray therapy. Such a procedure seems unjustified, for while removal of the hypophysis may suppress the ketogenesis and glycosuria of experimental diabetes, it does so only by superimposing a second metabolic abnormality upon that already existing.

#### RELATION TO BLOOD FORMATION

The liver stores substances which are essential for the normal formation of the red cell stroma (antipernicious anemia factor), hemoglobin (antisecondary anemia factor), and also stores iron. It also plays a large part in the formation of the blood proteins, especially fibrinogen and albumin, and is concerned in the production of those substances other than fibrinogen that are essential for the clotting mechanism. It is important for the regulation of the circulating blood volume and the prevention of excessive dilution after fluid administration.<sup>35</sup>

It has been shown by Ivy<sup>36</sup> that while the liver of the untreated pernicious anemia patient contains little or no anti-PA factor, storage may occur readily when liver extract is given. It is possible, however, that in liver disease the retention of this substance is diminished, for Rosenberg<sup>37</sup> has described a macrocytic anemia occurring in such cases that may be difficult to differentiate from pernicious anemia, and Goldhamer, Isaacs, and Sturgis<sup>38</sup> have found decreased storage of the anti-PA factor in cirrhosis. The anemia is seldom as severe as that which may occur in untreated pernicious anemia but is similar in type. Whipple and Robscheit-Robbins<sup>39</sup> find that the effectiveness of human liver in promoting hemoglobin formation (and hence presumably the storage of the antisecondary anemia factor) is much decreased by the presence of parenchymal injury. Thus it seems that while liver disease may decrease the storage of both factors, the more important effect is on the stroma-producing (anti-PA) substance, since the anemia that develops is of the primary type. The factor of safety that is present in the relation of the liver to blood formation, as in other liver functions, is illustrated by the observation of Daft, Whipple, and Robscheit-Robbins<sup>40</sup> that only in very severe or fatal experimental liver injury is there a decrease in hemoglobin formation, if iron is given intravenously.

The inability of the diseased liver to form blood proteins normally, as shown by Kaunitz,<sup>41</sup> Ipanov and Chervyakovski,<sup>42</sup> and Kasugai,<sup>43</sup> especially the decreased formation of albumin which results in a disturbance of the albumin-globulin ratio, seems to be the basis of the Takata-Ara reaction which was first used empirically. Unfortunately,

the Takata-Ara test is not as specific as might be desired, being positive in certain infectious diseases.

#### GENERAL CONSIDERATIONS

It is striking that so many types of liver injury (Eck fistula, ligation of common bile duct, bile fistula, hepatotoxins) are followed in many instances by ulcerations of the duodenum which are chronic and have many of the characteristics of human "peptic" ulcer. Correspondingly, most of the methods employed to produce experimental peptic ulcer seem to depend upon interference with hepatic function. Crandall and Ivy<sup>30</sup> have reviewed this apparent relationship between ulcer and liver damage and conclude that, while the question is still obscure, the evidence is so suggestive that further intensive study is indicated. In the same article these authors have discussed the relationship of liver disease and experimental injury to pathologic changes in the central nervous system.

Other functions of the liver, i.e., protein metabolism, vitamin storage, relation to mineral balance, pigment metabolism, etc., have undergone many advances in recent years but few clear cut clinical applications have been developed. It is not known how hepatic disease may affect the storage of vitamins A and D, although Knöpfelmacher and Reiter<sup>44</sup> were unable to show that liver injury decreased the conversion of carotene to vitamin A. Addis, Poo, and Lew<sup>45</sup> have shown that storage of protein occurs in the liver to a proportionately greater extent than in any other organ.

In conclusion we should again emphasize the importance to the surgeon in evaluating the degree of hepatic insufficiency that may be present before he undertakes any surgery upon the biliary tract. In view of the unfortunate accidents that so often complicate such operative procedures, it would seem that a preliminary evaluation of liver function is indicated. The bilirubin clearance<sup>46</sup> is perhaps the most sensitive test, although it is valueless in the presence of jaundice. If the hippuric acid test<sup>18</sup> is definitely positive or if the venous stasis bleeding time<sup>47</sup> is much prolonged, or if other tests show impairment of liver function, the increased surgical risk must be taken into consideration.

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## NONCALCULOUS CHOLECYSTITIS

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THERE is perhaps no disease which is more variable in the severity of symptoms manifested than is cholecystitis. Although gallstones are probably the most common type of lesion capable of producing symptoms, there are nevertheless numerous other types, much less clearly understood, which can produce serious trouble. It is likewise noteworthy that there is scarcely any other disease in which the relationship between the pathologic findings and amount of symptoms is so variable and inconstant. These features are largely responsible for the difficulty encountered in arriving at a decision relative to advisability of operation, etc., particularly in the noncalculous type of cholecystitis.

During recent years reasonably satisfactory proof has been offered of the existence of a new disease entity which has been called biliary dyskinesia, the principal feature of which is a spasm of the sphincter of Oddi. Acceptance of this new type of biliary disorder scarcely allows us to apply the term noncalculous cholecystitis to the entire group of patients to be discussed in this study because of the location of the offending lesion outside the gall bladder. However, there does not appear to be a better term available, particularly since most workers on this subject consider the term noncalculous cholecystitis an inclusive one.

For many years various authors, from time to time, have called attention to the fact that better results were to be expected (Judd,<sup>1</sup> Lahey,<sup>2</sup> and others) following cholecystectomy if symptoms were severe, i.e., of the nature of biliary colic. During the past few years it has become apparent, from various reports published, that the results of cholecystectomy (likewise cholecystostomy) are so unsatisfactory in patients with noncalculous cholecystitis that serious effort should be made to discriminate more closely as to when cholecystectomy should be advised. In a study of cholecystectomies for stoneless gall bladder, Graham and Mackey<sup>3</sup> noted that only 60 per cent of the patients considered themselves relieved of symptoms by the operation. In a similar study Lehman and his associates<sup>4</sup> noted that after cholecystectomy satisfactory results were obtained in 70 per cent of patients with stones; whereas in the patients without stones satisfactory results were obtained in only 64 per cent. The percentage of favorable results in the noncalculous group reported from each of these two

clinics is discouragingly low, but remarkably similar, and probably represents a fair estimate of the results obtained throughout the country in the noncalculous type of cholecystic disease. The seriousness of the poor surgical results in noncalculous cholecystitis becomes more apparent when we stop to realize that one-third to one-half of the cholecystectomies performed throughout the country are performed upon patients without gallstones. The realization that such a large percentage of patients submitted to cholecystectomy have a poor prognosis staring them in the face is sufficient to stimulate an enormous amount of thought and effort in an attempt to eliminate the poor results. It is obviously incorrect to discredit the operation of cholecystectomy on all patients without stones in their gall bladders, since it is well known that practically all the variations of pathologic processes, including even gangrene with perforation of the gall bladder, may be encountered in cholecystitis without stone. Analysis of the group of unfavorable results following cholecystectomy in noncalculous cholecystitis by numerous authors reveals the fact that the poorest results are obtained in the group with mild pathologic findings, in which there is no history of significant gall bladder pain or colic and perhaps a doubtful cholecystographic diagnosis, such as might be made on faintness of shadow. Graham and Mackey noted that in their group of stoneless cases 76 per cent of their patients giving a history of gall bladder colic were relieved; whereas only 58 per cent of those without colic sustained satisfactory results following cholecystectomy.

It is agreed by practically all observers, particularly those making a study of noncalculous cholecystitis during the past few years, that a large percentage of failures following cholecystectomies in patients without significant biliary colic is due to an *erroneous diagnosis*. This feature has been stressed by Wier and Snell,<sup>5</sup> Stanton,<sup>6</sup> and others, all of whom have repeatedly warned against the frequency of these errors in diagnosis. The fact remains, however, that the manifestations produced by the disease which have confused the issue, are often more typical of cholecystitis than the manifestations of many cases of proved cholecystitis. The situation is made much more complicated by the fact that cholecystitis, being such a frequent disease, is very apt to be encountered along with another disease which may be much more serious than the cholecystic disease itself. A list of the diseases with which cholecystitis may be confused is so limitless that their differential diagnosis cannot be considered here. The more common diseases in this group include such lesions as carcinoma of the colon, peptic ulcer, carcinoma of the stomach, pancreatitis, carcinoma of the pancreas, constipation, colitis, cirrhosis of the liver, intestinal allergy, tuberculosis of the spine, renal disease, etc.

## NONCALCULOUS CHOLECYSTITIS

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THERE is perhaps no disease which is more variable in the severity of symptoms manifested than is cholecystitis. Although gallstones are probably the most common type of lesion capable of producing symptoms, there are nevertheless numerous other types, much less clearly understood, which can produce serious trouble. It is likewise noteworthy that there is scarcely any other disease in which the relationship between the pathologic findings and amount of symptoms is so variable and inconstant. These features are largely responsible for the difficulty encountered in arriving at a decision relative to advisability of operation, etc., particularly in the noncalculous type of cholecystitis.

During recent years reasonably satisfactory proof has been offered of the existence of a new disease entity which has been called biliary dyskinesia, the principal feature of which is a spasm of the sphincter of Oddi. Acceptance of this new type of biliary disorder scarcely allows us to apply the term *noncalculous cholecystitis* to the entire group of patients to be discussed in this study because of the location of the offending lesion outside the gall bladder. However, there does not appear to be a better term available, particularly since most workers on this subject consider the term *noncalculous cholecystitis* an inclusive one.

For many years various authors, from time to time, have called attention to the fact that better results were to be expected (Judd,<sup>1</sup> Lahey,<sup>2</sup> and others) following cholecystectomy if symptoms were severe, i.e., of the nature of biliary colic. During the past few years it has become apparent, from various reports published, that the results of cholecystectomy (likewise cholecystostomy) are so unsatisfactory in patients with noncalculous cholecystitis that serious effort should be made to discriminate more closely as to when cholecystectomy should be advised. In a study of cholecystectomies for stoneless gall bladder, Graham and Mackey<sup>3</sup> noted that only 60 per cent of the patients considered themselves relieved of symptoms by the operation. In a similar study Lehman and his associates<sup>4</sup> noted that after cholecystectomy satisfactory results were obtained in 70 per cent of patients with stones; whereas in the patients without stones satisfactory results were obtained in only 64 per cent. The percentage of favorable results in the noncalculous group reported from each of these two

marily of bacterial origin. Andrews<sup>9</sup> has noted that acute cholecystitis can be produced experimentally by injecting bile into the gall bladder "in concentrations only one or two per cent more than the six or eight that are found in normal human bile." The fact that cholecystectomy can be performed in the presence of acute cholecystitis with a relatively low mortality and without development of infection supports the idea that infection is by no means the only important mechanism in the pathogenesis of acute cholecystitis.

The manifestations produced by acute noncalculous cholecystitis are so slightly different from those produced by acute calculous cholecystitis that they need not be described in detail here.

However, in a recent report Wolfson and Rothenberg<sup>10</sup> remark that patients with noncalculous acute cholecystitis "appear sicker, more frequently have chills, and maintain a higher temperature range than those with acute cholecystitis caused by cystic duct stone." They noted also that dyspepsia, belching, aversion for fatty food, and a history of previous attacks were not as common in patients with acute noncalculous cholecystitis as in those with acute calculous cholecystitis. The above-mentioned differences will not be constant enough, however, to be of great value in the determination of presence or absence of stones in the gall bladder when an acute inflammation is present. Perforation of the abdominal wall secondary to gall bladder disease is perhaps an exception to this statement since stones or carcinoma are usually present when this happens; in the latter instance, i.e., carcinoma, stones likewise are present.

2. *Chronic Inflammation.*—Obviously on many occasions chronic cholecystitis is the direct result of a partial subsidence of an acute cholecystitis, regardless of the primary factor. On some occasions the adhesions which were a direct result of the acute inflammation are the only residue of the inflammation. These may or may not be a residue of chronic inflammation throughout the adhesions and scarred areas and symptoms may or may not be produced by them. In reality then, on many occasions healing has taken place quite completely and the adhesions represent merely a scar, just as a scar forms on the skin after a laceration or infection heals. The term pericholecystitis has been assigned very appropriately to this lesion. Although experience has taught us that many gall bladders with pericholecystic adhesions will function properly as far as concentration (as determined by cholecystography) is concerned, yet a large percentage of individuals in whom pericholecystitis has been found will complain of dyspepsia or colicky pain or both. Pericholecystitis produced by lesions outside the gall bladder (e.g., duodenal ulcer) is perhaps slightly less apt to produce symptoms because there is no involvement of the cystic duct or mucosa and submucosa of the gall bladder.

Stanton has made a particular study of the patients in his series upon whom the diagnosis was incorrectly made. In his series of cholecystectomies he noted that of 90 patients followed for a period of years only 67 (or 74.5 per cent) made a complete recovery. Moreover, in this group of 67 cases obtaining relief from cholecystectomy, the diagnosis was discovered to be erroneous in 19. I am inclined likewise to believe that an erroneous diagnosis explains the majority of poor results and I doubt that actual figures in other clinics would differ significantly from those of Stanton.

It cannot be disputed, however, that there is a large group of patients suffering from noncalculous cholecystic disease who are relieved by cholecystectomy. This group must not be deprived of the relief which may be offered them. As already stated, we must learn to differentiate the favorable from the unfavorable group and we must learn not to operate on the group which previously has yielded such poor results.

#### TYPES OF LESIONS ENCOUNTERED IN NONCALCULOUS CHOLECYSTITIS

The types of noncalculous lesions of the gall bladder capable of producing symptoms can be divided into six groups; one of these groups (cholesterosis), as will be pointed out, may be insignificant in the production of actual symptoms. Because of the wide variation in manifestations and uncertainty as to whether the pathogenesis of acute and chronic inflammation is the same, these two lesions will be considered separately.

1. *Acute Inflammation*.—Practically every phase of acute cholecystitis associated with calculi may be found in acute noncalculous cholecystitis. The actual mechanics of the production of the acute inflammation are no doubt different in calculous and noncalculous cholecystitis, but the pathologic and clinical results may be quite identical. Nevertheless, it is a well-known fact that the majority of patients suffering from acute cholecystitis have gallstones. This implies, and correctly so, that stones are a very important factor in the pathogenesis of acute cholecystitis.

In a series of 38 patients with gangrenous cholecystitis reported by Mentzer,<sup>7</sup> 10 cases were noncalculous in origin. In a study of 160 cases of acute cholecystitis Whipple<sup>8</sup> noted that 30 (18 per cent) had no stones. However, an analysis of numerous reports in the literature scarcely bears out such a high figure; it is doubtful if more than 10 per cent of patients with acute cholecystitis have no stones in their gall bladder.

Bacteriologic studies made from the wall and lumen of the acutely inflamed gall bladder persistently have revealed a surprisingly low percentage of positive cultures (somewhat greater than 50 per cent). This fact has led certain observers (Denton and Feinbatt) to suspect that in a huge percentage of instances acute cholecystitis was not pri-

clinical grounds is impossible. This difficulty is particularly significant if an obstruction is present at the cystic duct.

3. *Lesions of the Cystic Duct.*—When deformities of the cystic duct were emphasized many years ago as being important factors in the pathogenesis of gall bladder disease (Schmieden and Rohde<sup>13</sup> and Seelig<sup>14</sup>), the theory was accepted quite wholeheartedly, particularly in noncalculous cholecystitis. However, detailed study showed fallacies in such an explanation in a large percentage of cases. During recent years the pendulum of thought is swinging far over to the theory that dysfunction or spasm of the sphincter (biliary dyskinesia) will explain the pathogenesis in the entire group of noncalculous gall bladder disease. I am willing to accept the theory of biliary dyskinesia, but for several reasons I wish decisively to issue caution in attempting to explain the vast majority of cases of noncalculous disease on this theory. A wholehearted acceptance of biliary dyskinesia as the explanation of pathogenesis of noncalculous cholecystitis would preclude the acceptance of the data advanced during the past three or four years, that obstruction of the cystic duct is a very important primary factor in the formation of gallstones. This feature in the pathogenesis of gallstones seems to have too much foundation to allow total discredit. Last, on many occasions obstruction to the cystic duct may be unmistakable and may even be so severe as to produce a complete obstruction. Since adhesions surrounding a structure as large as an intestine can produce obstruction, why could not adhesions, which are frequently so dense about the cystic duct as to require sharp dissection, likewise cause obstruction to a lumen which is many times smaller?

Caution also must be exercised in applying the theory of cystic duct obstruction to the explanation of symptoms in a wholesale manner in gall bladder disease, but the three patients to be described appear to illustrate three of the important types of obstruction; viz., angulation of the duct, stenosis, and anomalous excessive Heisterian folds. True enough, no positive proof can be offered that lesions of the cystic duct as described in these three patients were the primary cause of the patient's complaints. Nevertheless the wall of each gall bladder was so slightly diseased and the common duct appeared so normal that we feel justified in suspecting the cystic duct as being the major factor in the production of the patient's complaints. It is quite true that two of the three patients had a pericholecystitis, which was probably secondary to previous cholecystostomy, but there is a growing tendency to attach less importance to pericholecystitis in the production of symptoms than we did a few years ago. The two patients having a previous cholecystostomy demonstrate very clearly the inefficiency of that operation. Each of the three patients whose protocols are given had an unusual amount of fat and fibrous tissue deposited about the

In the majority of instances chronic noncalculous cholecystitis, as characterized primarily by thickening of the gall bladder wall and lymphocytic infiltration, does not arise as a sequel of acute inflammation but develops insidiously. From the standpoint of deleterious effects on the patient, it makes no difference whether the inflammation is of chemical or bacterial origin. The mechanism of the development of the bacterial type of inflammation has been presented by Graham and Peterman<sup>11</sup> and others. In either the chemical or bacterial chronic cholecystitis the wall may be so badly damaged as to destroy practically entirely the function of the gall bladder, particularly when we consider that the region about the cystic duct likewise becomes involved not only by edema but by actual inflammatory tissue such as lymphocytic infiltration, scar tissue, etc.

The importance of Wolfer's<sup>12</sup> experiments, showing that in dogs a cholecystitis (which is demonstrable months after its initial production) may be induced by pancreatic juice, has not been adequately recognized in the pathogenesis of cholecystitis. Wolfer found experimentally that an appreciable portion of pancreatic juice injected into the common duct or allowed to enter the common duct by a reflux resulting from mechanical intubation of the two ducts, so that a common channel was established, could be found later in the gall bladder. In either case a definite cholecystitis would result, presumably produced by the irritative action of the pancreatic secretion. It has been shown by numerous observers that the secretory pressure of the pancreas is greater than that of the liver. One can readily see then that in the human being any obstruction at this sphincter of Oddi distal to the junction of the choledochus and the duct of Wirsung, regardless of whether it was produced by stone or spasm, might allow the entrance of pancreatic secretion into the common duct and gall bladder with subsequent production of a cholecystitis.

In a small percentage of people there is such a significant variation in the size and course of the cystic duct that the slightest edema or scarring at this point would lead to serious obstruction to the inflow and outflow of bile, the latter of which is perhaps of more importance from the standpoint of production of symptoms. The actual importance of noncalculous cholecystitis becomes more obvious when we consider the suggestions of Andrews, Phemister, and others that, in general, cholesterol stones are produced by short periods of obstruction at the cystic duct and calcium stones produced by long periods of obstruction. Obviously the primary factor under these circumstances would have to be noncalculous in origin.

Although, as a general rule, the patients with calculous cholecystitis are apt to complain of more severe symptoms than patients with noncalculous cholecystitis, experience has taught us that in many instances the manifestations may be so similar that a differentiation on pure

The angulation of the cystic duct in the patient described above was very pronounced (Fig. 1A). The valvular folds of Heister were not unusually prominent, but there was such a profuse amount of fatty and fibrous tissue deposited around this duct that the slightest edema, particularly at the point of angulation, would certainly have produced an interference with filling and emptying. The cholecystogram, as noted in Fig. 2, revealed a shadow of practically normal intensity. There was evidence of contraction after the fat meal, but emptying appeared to be definitely though not severely delayed. Delay in emptying is thought by many observers to be indicative of a definite disease process, but I am perhaps less convinced than the average observer that we can use this finding as a deciding factor indicating sufficient pathologic damage to justify cholecystectomy.



Fig. 2.—Cholecystogram of Case 1 (see Fig. 1A). A, Shadow of normal density, sixteen hours after oral administration of the dye but revealing a deformity which is presumably secondary to a previous cholecystectomy. B, Film taken seventy minutes after fat meal shows a slight decrease in size, but a definite retardation in emptying following the fat meal. Previous to this study, the author was inclined to minimize the significance of delayed emptying, but Cases 1 and 2 suggest that obstruction of the cystic duct may act as a mechanical factor in producing a delay in emptying.

The value of the cholecystogram in this instance is doubtful unless the delay in emptying and deformity of the shadow are considered to be indicative of a pathologic gall bladder. The patient noted that cholecystectomy had relieved her symptoms, but, as only a few months have intervened since operation, judgment on result must be deferred. The patient had typical symptoms of gall bladder colic; since operative results are so satisfactory in this group of patients, we feel quite confident that the relief from symptoms will persist.

CASE 2.—Patient was a woman, aged forty-six years; she had a cholecystostomy performed one year before entrance because of pain in the right upper quadrant. For six months she was free from pain. After this interval, however, pain began



cystic duct, indicating that the periductal region had been the site of considerable inflammation at some previous time. Perhaps the densest periductal adhesions were encountered in Case 2, in which the stenosed cystic duct with a tiny lumen was noted.

#### CASE REPORTS

CASE 1.—Patient was a woman, aged 38 years; she had had a cholecystostomy performed in 1925 because of pain in the right upper quadrant and epigastrium. Symptoms were relieved up until one year before entrance to the hospital. At that time she noticed the development of a steady, gnawing pain in the epigastrium which became colicky in nature and radiated to the right upper quadrant and posteriorly. She has had numerous attacks during the past year; during the attacks of pain she was nauseated and vomited frequently. Between the attacks of pain she complained of chronic dyspepsia. For the past several months she has had pain accompanied by vomiting almost every day.

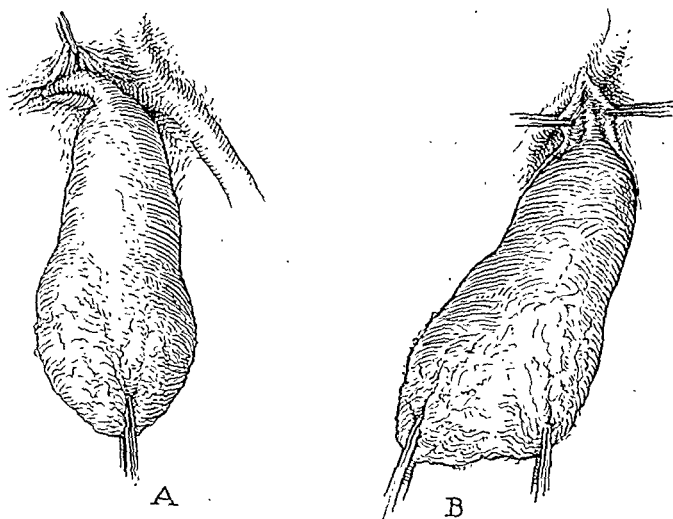


Fig. 1.—Two types of lesions at the cystic duct which are capable of creating serious interference with the proper passage of bile into and out of the gall bladder. A, Nothing was found at operation to explain the typical attacks of gall bladder colic (see Case 1) except the marked angulation as illustrated. The adhesions were so dense at this point that fixation must have been complete. Cholecystograms indicate that the gall bladder could fill (see Fig. 2) but could not empty properly, presumably because of the obstruction at the cystic duct. B, Symptoms of this patient (Case 2) were also those of a fairly typical gall bladder colic. The only operative findings which might explain the patient's symptoms were referable to the cystic duct which was stenosed and surrounded with very dense adhesions.

Examination revealed tenderness in the right upper quadrant and epigastrium of equal intensity, but no appreciable muscle spasm. The temperature was normal. The leucocyte count was 13,800. Cholecystograms revealed a shadow of almost normal density but distinctly deformed, presumably because of the previous cholecystectomy. After the fat meal the gall bladder contracted but showed a definite delay in emptying (Fig. 2). At operation the gall bladder was found to be moderately adherent to the anterior abdominal wall and surrounding organs, but the wall of the gall bladder was not thickened except at the dome, where there was a scar of a previously performed cholecystostomy. The cystic duct was buried in fatty and fibrous tissue. When it was dissected out, a sharp angulation in the cystic duct was noted. The common duct was normal in size. There were no stones in the common duct or gall bladder.

the Heisterian folds traverse the mucosal surface of the cystic duct in a spiral fashion thereby facilitating the flow of bile. The anomalous position of a mucosal fold transversely across the lumen of the cystic duct obviously would offer a greater obstruction to the passage of bile than a spiral location. Only the proximal portion of the cystic duct was removed; we, therefore, do not know whether the remainder of the folds were anomalous or not. Even a mild inflammation of the cystic duct, with its resultant edema, would almost certainly offer serious obstruction. Such a local process, i.e., inflammation with edema and subsequent blockage of the duct, would possibly explain the attack which the patient had three months previous to admission and the

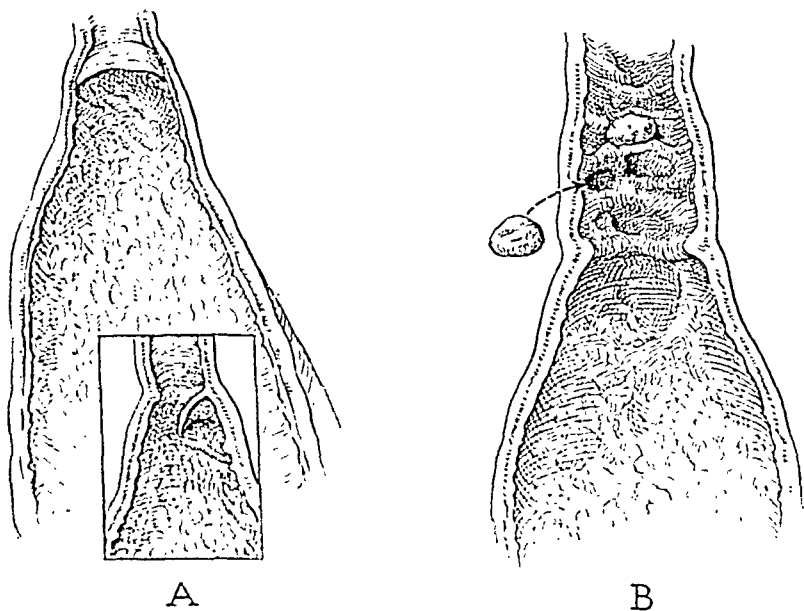


Fig. 3.—Transverse folds of Heister are anomalous and are not consistent with proper flow of bile into and out of the gall bladder, particularly the latter. *A*, Transverse cup-shaped fold found in the cystic duct of a patient (Case 3) who had symptoms for three months and whose cholecystogram revealed no shadow. It is obvious that even slight edema of the fold or wall of the cystic duct might impair exchange of bile, particularly the outflow, as illustrated more clearly by the insert. *B*, This gall bladder with transverse Heisterian folds between which two small stones were solidly imbedded is shown to illustrate perhaps a later stage in the ill effects incident to transverse folds: It is true, however, that stones may lodge in the cystic duct regardless of the configuration of the duct.

dyspeptic symptoms retained since then. The cup-shaped fold, with the concavity facing the fundus, would act as a valve and would tend to offer obstruction to emptying perhaps more readily than filling, but apparently obstructed flow in either direction, since cholecystograms showed no shadow. The wall of the fundus of the gall bladder showed so few pathologic changes that it can scarcely be blamed for the absence of a cholecystographie shadow; a finding which in our hands is quite reliable as an indication of serious gall bladder disease. Our

to return in attacks. Pain was moderately severe, of a colicky nature, and not associated with eating. Very little dyspepsia was noted between meals. Examination revealed tenderness in the right upper quadrant with very slight muscle spasm. The leucocyte count was 6,000. Cholecystograms revealed a distorted shadow which was less dense than normal. At operation there were numerous adhesions about the gall bladder but none of them were very dense. The gall bladder wall was not appreciably thickened. The cystic duct was buried in fatty and fibrous tissue and when dissected out was found to be unusually small, and appeared not to be patent; but examination later revealed bile in the lumen of the gall bladder. Cholecystectomy was performed. No stones were found in the gall bladder.

There is a rather marked similarity between the history, physical findings, etc., in Cases 1 and 2. In each instance the gall bladder wall was only slightly diseased, but the angulation of the cystic duct in one patient and the stenosis in the second were so pronounced that there must have been considerable obstruction to the passage of bile in and out of the gall bladder. The fatty and fibrous deposit around the cystic duct in Case 2 was so dense that the existence of acute inflammation at some previous time seemed obvious. The history of frequent attacks of pain in these two patients might support the supposition that stones were present in the gall bladder; the absence of stones supports the fallacy of attempting to predict the type of pathologic findings from the clinical findings. The most reliable data from the standpoint of predicting the type of pathology in these two patients lie in the cholecystographic findings which indicate that, although pericholecystitis exists, the wall of the gall bladder is not seriously diseased and that the cystic duct is sufficiently patent to allow passage of bile through it, although the cholecystographic shadow is less dense than normal.

CASE 3.—The patient was a man, aged 37 years, who was apparently entirely well until three months before admission to hospital. At this time he noticed a steady aching pain in the epigastrium following a heavy meal. Pain did not radiate. He vomited two or three times during the first day or two. Pain lasted six days and gradually decreased. Since then he has noted that when he eats fried or greasy foods the pain reappears. Recently the pain has been relatively constant and confined to the epigastrium and right upper quadrant. Examination revealed tenderness without muscle spasm in the right upper quadrant, with a decreased amount of tenderness in the epigastrium. The temperature was normal. The leucocyte count was 9,900. Cholecystograms revealed no shadow of the gall bladder. At operation, by Dr. Puestow, the gall bladder wall was found to be only moderately thickened, with a few adhesions about the organ. Because of the absence of shadow on the cholecystogram, however, it was removed. Upon opening the gall bladder, a cup-shaped, transverse, thin, valvular fold was found in the proximal portion of the cystic duct. No stones were found.

The cup-shaped transverse valvular fold noted at the proximal portion of the cystic duct, as shown in Fig. 3A, was remarkably thin for a Heisterian fold but projected so far into the lumen of the cystic duct that it obviously offered definite obstruction to the duct. Ordinarily

Ileocechus is separate from the duodenal musculature and is of sufficient size that hypertrophy or overstimulation might be capable of giving rise to biliary stasis.

At the present time there is considerable discussion as to what group of patients can be classified as belonging to the syndrome of biliary dyskinesia. Part of the difficulty and confusion is readily explained if we accept Westphal's classification into two types: (1) cases in which the vagus is oversensitive (parasympathetic predominance), resulting in hypermotility or hypertonicity with rapid emptying of the gall bladder accompanied by spasm of the ampulla of Vater; and (2) cases in which the vagus is undersensitive (sympathetic predominance), creating atony of the gall bladder and ampulla with spasm of the sphincter of Oddi. However, in each type the final important disturbance is blockage of bile flow. Although it appears that the paralysis of the sphincter of Oddi as noted after cholecystectomy is usually permanent (Puestow<sup>25</sup>), instances have been reported, as mentioned previously, when a spasm of the sphincter of Oddi was noted postoperatively. It is apparent that this spasm may be responsible for the patient's symptoms and failure to obtain relief. It is barely possible that in many instances relief of symptoms following operation (cholecystectomy) is dependent upon a paralysis of the sphincter of Oddi. It appears that this group of patients who have persistent symptoms following cholecystectomy and in whom spasm of the sphincter is demonstrable may be classified in the group of biliary dyskinesia.

Newman<sup>17</sup> has classified the cases clinically into two groups. To those having spastic distention of the gall bladder he ascribes symptoms of "pain, of a dull grinding character coming on in spasms like colic but not so severe, and lasting for many minutes at a time." This pain may spread across the abdomen to the left or radiate backward on the right. A feeling of fullness, nausea, anorexia, occasional vomiting may be complained of. The gall bladder is able to concentrate normally but empties slowly. In the group having atonic distention, Newman classifies patients usually thin in stature, complaining of continuous not spasmodic pain coming on soon after meals and radiating all over the epigastrium but not to the back. Anorexia is present along with occasional vomiting but little nausea. Cholecystography "shows a very long thin gall bladder, which throws a poor shadow and empties very little." In the spastic distention type Newman reports favorable success in treatment with diet and belladonna, but he reports poor success in the atonic distention type.

5. *Metabolic Disturbances in the Biliary System.*—It seems likely that most of the pathologic metabolic findings are of importance chiefly in relation to the ultimate production of stones or to the deposition

attention therefore is turned to the cystic duct, particularly since the common duct appeared normal and an obvious lesion was found in the cystic duct. Microscopic examination revealed a thickening and slight fibrosis of the wall of the cystic duct, but it is futile to attempt to determine how much fibrosis in a cystic duct is required to produce an obstruction with so many variable features, such as size of the lumen, thickness of bile, etc. To support the contention that a transverse fold as shown in Fig. 3A may be a potential source of serious difficulty, a drawing of another gall bladder with two small stones lodged between transverse folds in a cystic duct is shown in Fig. 3B.

4. *Biliary Dyskinesia*.—As already stated, if the theory of biliary dyskinesia as popularized by Westphal<sup>15</sup> and supported by the work of Ivy,<sup>16</sup> Newman,<sup>17</sup> and others is accepted as a clinical fact, it would offer a satisfactory explanation for the symptoms produced in a large percentage of patients with noncalculous "cholecystitis." Under normal circumstances the secretory pressure of bile by the liver, which varies between 300 and 360 mm. of water (Judd and Mann<sup>18</sup>), is far above the 100 mm. water (experimental in dogs) necessary to break through the sphincter of Oddi (Cole,<sup>19</sup> 1925). Although there is usually a fairly complete paralysis of the sphincter following cholecystectomy (Puestow<sup>20</sup>), occasional instances have been reported (Walters and associates,<sup>21</sup> Doubilet and Colp<sup>22</sup>) when sufficient spasm of the sphincter of Oddi has been noted postoperatively to produce symptoms and to require a pressure of 160 mm. of water to break through it. In such instances, the pain complained of is similar or identical to that noted before operation. Nitroglycerin (glyceryl trinitrate) relieves the pain<sup>21</sup> produced by this spasm.

Ivy and associates<sup>23</sup> have recorded some experimental findings on human subjects which support the existence of spasm of the sphincter of Oddi and its relation to distress in the right upper quadrant. During the process of draining the bile from a human subject by means of a duodenal tube, distress in the right hypochondrium was experienced simultaneously with cessation of drainage of bile. This distress in the right hypochondrium was increased by the injection of secretin, cholecystokinin, and was relieved by the introduction of magnesium sulfate through the tube. It is obviously important to find out what physiologic or pathologic factors are capable of producing spasm of the sphincter and what relation the spasm has to the production of symptoms. Walters and associates have observed that the rise in pressure within the common duct from 0 to 200 to 350 mm. water, as produced by the hypodermic injection of morphine, may at times be associated with pain in the upper abdomen. This pain and discomfort is not unlike that experienced by many patients with supposed gall bladder disease. Boyden<sup>24</sup> recently has shown that the sphincter cho.

# SUMMARY

During the past several years, a few rather radical changes in our ideas relative to the pathogenesis of gall bladder disease and the mechanism of production of symptoms have been developed. The theory of production of certain types of gallstones by obstruction of the cystic duct, the theory of production of acute inflammation of the gall bladder by chemical means, and the supposition that biliary dyskinesia is responsible for the pain in many cases of so-called cholecystitis are the three most important developments in this regard. When the possibility of production of gall bladder disease by obstruction of the cystic duct was introduced many years ago, it received wholehearted support, but some observers have ventured to entirely discredit this possibility. I contend that there are many cases of so-called cholecystitis which are dependent upon obstruction of the cystic duct for the manifestations produced and that this theory in the pathogenesis of gall bladder disease by no means can be dropped entirely. Severe angulation, stenosis of the duct and anomalous valvular folds seem to be capable of producing symptoms which are so serious as to demand relief.

It appears that biliary dyskinesia may explain symptoms in a few patients with manifestations of cholecystitis, particularly in the group which does not obtain relief following cholecystectomy. According to present reports, some of these patients complain of severe symptoms described as gall bladder colic; whereas, others complain of mild symptoms, such as dyspepsia, etc. Part of this confusion no doubt is due to the fact that the term is used too inclusively. There is scarcely any doubt that spasm of the sphincter of Oddi, when it does exist, occurs much more frequently as an entity secondary to stones in the common duct, pancreatitis, or some other organic lesion, than it does as a spasm primarily of neuromuscular origin. Extreme caution must therefore be exercised lest too much attention is directed therapeutically to relieving the spasm rather than to treatment of the lesion responsible for the spasm.

For the time being it would appear appropriate to reserve the diagnosis of biliary dyskinesia for a small group of cases, utilizing the diagnosis and therapeutic procedures advocated by Walters, Best and Hicken,<sup>31</sup> and others. It appears logical to assume that no single factor is responsible for cholecystitis. Many factors, including acute and chronic infection of the gall bladder, chemical inflammation, obstruction of the cystic duct, biliary dyskinesia, and perhaps others, are important in the pathogenesis of gall bladder disease.

At the present time it is practically impossible to differentiate patients with cholecystic manifestations so accurately as to eliminate

of calcium in the wall of the gall bladder. Fowweather and Collinson<sup>26</sup> and Ravdin and associates<sup>27</sup> have noted that in hydrops of the gall bladder a high concentration of calcium was demonstrable in the contents of the gall bladder. Phemister and associates<sup>28</sup> have emphasized the relationship of chronic obstruction of the cystic duct to the formation of calcium stones and the deposition of calcium in the gall bladder wall. Although in Phemister's series the obstruction in the cystic duct was found to be produced by a stone, other observers have reported the association of calcium stones with obstruction of the cystic duct produced by fibrosis. It appears likely, however, that the metabolic disturbances associated with the formation of the stones as noted above were secondary perhaps to an obstruction at the cystic duct. This obstruction, which of necessity must be of a chronic nature, may be due to scar tissue produced by inflammation or due to anomalous valvular folds which might likewise produce obstruction, particularly if the cystic duct becomes involved in any inflammatory process.

The importance of the change in the bile salt-cholesterol ratio in the etiology of cholesterol stones has been emphasized by Andrews and associates.<sup>29</sup>

When we take into consideration the fact that a very slight increase in the concentration of bile salts in bile may produce an acute cholecystitis experimentally (Andrews), we can readily see that metabolic disturbances may be extremely important in the development of acute and chronic cholecystitis. It is probable that there are many more such metabolic disturbances which are important in the pathogenesis of cholecystitis and that they unfortunately are not as simple as this one mechanism.

6. *Cholesterosis*.—As stated previously there is a growing disbelief in the relationship<sup>9, 30</sup> between cholesterosis and symptoms of gall bladder disease. In the first place the condition is encountered frequently in animals (particularly the dog) in which no other manifestations of gall bladder disease are noted. Moreover, it is seen frequently at the autopsy table in patients who had no manifestations of gall bladder disease during life, implying that its appearance in the presence of definite pathologic lesions in the gall bladder or biliary tract may be of little significance. Gallstones will be found to accompany cholesterosis in one-third to one-half of the occasions when it is noted at the operating table. It is quite true that the results of cholecystectomy in such instances are very satisfactory, but it is particularly noteworthy that excision of the gall bladder in the presence of cholesterosis without stones is accompanied by poor results. Considering the above data, it is therefore doubtful if cholesterosis has anything to do with the production of manifestations attributable to disease of the gall bladder.

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entirely surgical failures by declining operative procedures in the proper cases. One of the most common sources of surgical failure, and perhaps the most easily remedied, is the large group of patients in whom the diagnosis is grossly erroneous; i.e., the patient does not have cholecystitis but is suffering from a disease, such as carcinoma of the colon, arthritis of the spine, colitis, etc. In addition we must constantly bear in mind the fact that gall bladder disease may be present, though silent, and that the symptoms produced by the disease actually responsible for the patient's complaints may resemble those of gall bladder disease so closely that differentiation is extremely difficult. Removal of the gall bladder in these instances obviously will not relieve the patient's symptoms. In other words, all patients with gall bladder disease must be examined very thoroughly for the possible presence of another lesion in the upper abdomen or spine which may produce manifestations similar to those produced by cholecystitis. The greatest difficulty experienced at the present time in differential diagnosis lies in differentiation of patients with biliary dyskinesia and those actually having gall bladder disease. Because of the marked similarity of symptoms produced by the two conditions, it is doubtful if differentiation can be made on this basis alone. The fact still remains, however, that operation should be avoided in the group of patients complaining of only mild pain or distress and in those with doubtful cholecystographic evidence of disease.

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# ROENTGEN DIAGNOSIS OF SURGICAL DISEASES OF THE LIVER AND BILIARY TRACT

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**S**URGICAL diagnosis owes much to the notable achievements of Wilhelm Konrad Röntgen. His discovery and the accomplishments of those who followed him have presented a method which is constantly disclosing more and more of the unknown. This applies particularly to the roentgen diagnosis of surgical diseases of the liver and biliary tract. The development of this highly important field may be divided into three periods.

The first of these eras covered about fourteen years, from the discovery of the roentgen ray to the evolution of methods for examining the stomach and duodenum by the opaque meal. During this early period, interest was centered chiefly around the demonstration of opaque gallstones in the living patient. Buxbaum<sup>18</sup> reported opaque gallstone shadows in 1898 and Beck<sup>8</sup> in this country did likewise in 1900. Results were not encouraging, however, on account of the low incidence of opaque stones.

In the second period of development indirect evidence of gall-bladder disease was demonstrated by roentgen examination of the stomach and duodenum. Schürmayer<sup>76</sup> is credited with directing attention to signs of inflammation in the gall-bladder region by fixation or distortion of the visualized duodenum. Those who made a careful study of the problem were even more impressed by this evidence of gall-bladder dysfunction than by the presence or absence of opaque gallstones. Nevertheless, the limitations of the method in diagnosing any abnormalities of the biliary tract were all too obvious.

The third interval, from 1923 to the present time, may well be called the era of contrast media. The outstanding feature of this period is the work of Graham and Cole.<sup>30, 31</sup> These men were able to demonstrate, roentgenographically, the function and the anatomy of the biliary system by means of an intravenous injection of sodium tetraiodophenolphthalein. This new method was seized upon by roentgenologists everywhere and, without doubt, now constitutes one of the most valuable procedures in the diagnosis of disease of the biliary tract.

Further assistance has been gained in the visualization of the soft tissue shadows in the abdomen by means of diagnostic pneumoperi-

toneum. The use of halogenated oils and other opaque media to outline the biliary tract postoperatively and later the demonstration of the parenchymal shadow of the liver by the intravenous injection of thorium have increased the value of roentgen diagnosis of diseases of the liver and biliary tract.

#### ROENTGEN ANATOMY OF THE LIVER AND BILIARY TRACT

The position of the liver in a normal patient can be established in a posteroanterior roentgenogram of good technical quality. The liver appears as a large, homogeneous shadow in the right upper abdomen.

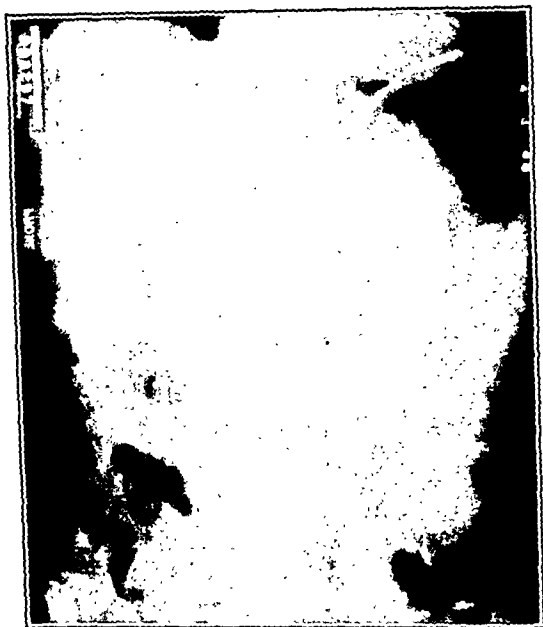


Fig. 1.—Enlarged liver. The borders of the liver are outlined by gas in the stomach and colon.

This shadow is partly superimposed by the shadows of the lower ribs. The general contour of the liver at times may be more or less outlined by shadows of gas in the stomach, duodenum, or colon (Fig. 1). The upper border of the right lobe of the liver corresponds to the dome of the diaphragm. The lower border may present two distinct lines, one conforming with the posteroinferior border and the other delineating the anteroinferior edge. The shadow of the inferior border may fade gradually into the shadow of the surrounding soft tissues without any definite line of demarcation. The right border approximates the inner aspect of the right lateral abdominal wall and frequently is not identified in its entirety. The left lobe of the liver is not readily seen because of its position in front of the spine.

In the lateral view the superior border of the liver can be seen as a curved line which is highest anteriorly. The inferior border cannot be identified with ease in this position.

The relation of the stomach, duodenum, and colon to the liver can be well demonstrated only after the use of a contrast medium. The importance of the anatomic position of these structures to that of the gall bladder is well shown by the combined use of cholecystography and the oral opaque meal (Figs. 2 and 3). Considerable variation in the relation of the structures in the right upper abdomen occurs frequently in the normal individual, depending upon body build and weight, the position of the patient at the time of roentgenography, the stage of respiration, and the amount of intra-abdominal pressure.



Fig. 2.

Fig. 2.—Anatomic relations of the gall bladder, stomach, and duodenum. Prone, oblique position showing pyloric antrum, partially filled duodenal bulb, and the gall bladder in an asthenic type patient.



Fig. 3.

Fig. 3.—Anatomic relations of gall bladder, stomach, and duodenum. Prone position in hypersthenic individual.

It is well known that hypersthenic or fat persons have a high liver; whereas, the asthenic or thin patient may show a liver which is low or rotated. The liver may move from 2 to 4 cm. with normal respiration. This free mobility can be well demonstrated in films taken in the erect and supine postures.

Measurements of the liver by means of the roentgen ray have been given by Pfahler,<sup>61</sup> Feldman,<sup>21</sup> and others. The former author noted an average total vertical measurement of the right lobe as 21.3 cm., with an average anteroposterior diameter of 12.8 cm. Such figures

are of little significance in the diagnosis of disease of the liver, although marked variations in its size are of considerable importance. An interesting observation of some practical application has been pointed out by Osgood and Habbe<sup>56</sup> in their roentgen study of fifty-three palpable and fifty-three nonpalpable livers. They noted that, in almost all cases, the inferior margin of the liver lies at least several centimeters below the right costal margin, provided that the film is exposed on deep inspiration with the patient in the horizontal position. The palpability of the liver, therefore, depends upon other factors; namely, the firmness of its lower edge, the position of the edge in relation to the palpating fingers, and the amount of rotation which may be present. Moody and van Nuys<sup>52</sup> indicate that long livers, with their lower tip as much as 5.0 cm. below the interiliac line, may be normal. They found sex to be a factor in their series, with more men than women showing long livers.



Fig. 4.—Position of gall bladder in lateral view.

The gall bladder occupies a position which varies markedly in normal individuals. Such variations depend largely upon the position of the patient during the roentgen exposure, the general anatomic type of the patient, the tonus of the gall bladder, and the position of the adjacent organs. With the patient in the dorsal decubitus (supine) position, the gall bladder may lie obliquely, with the fundus directed downward and laterally, just beneath the inferior border of the liver, or it may be seen in the plane at right angles with the long axis of the spine. In the erect posture the gall bladder usually assumes a more vertical position. It may project well beyond the inferior border of the liver, with the fundus of the gall bladder well below the interiliac line. In the ventral decubitus (prone) posture the fundus may be directed obliquely downward, outward and anteriorly, in the average 150-pound patient. In fat or hypersthenic persons the fundus may be directed laterally; whereas, in thin persons it may be directed

downward and, at times, superimposed by the shadow of the vertebral column. In the lateral view the gall bladder should be well anterior to the spine (Fig. 4).

The anatomic components of the normal gall bladder can be distinguished in the cholecystogram. Occasionally it is possible to see the cystic and common duct in the cholecystogram made after the administration of a fatty meal.

#### DIAGNOSIS OF DISEASES OF THE LIVER

The roentgen examination may be valuable in the demonstration of many lesions involving the liver. Such assistance, however, is dependent upon certain factors which may be introduced as an aid in diagnosis or which may be present as a result of disease. These factors



Fig. 5.—Calcification in the liver. Due to a large echinococcus cyst. (Courtesy of Dr. Herman Ostrum.)

include: (1) variations in density, such as calcification, gas shadows, fluid levels, or opaque media; and (2) variations in size, shape, or position of the liver itself or of its neighboring organs, visualized with or without opaque media.

Calcification in the liver is not common and occurs mostly as calcium carbonate and phosphate. When present, it is more often in centrally necrosed lobules, but it has been observed in Glisson's capsule in cases of nephritis.<sup>41</sup> Although evidence of such calcifications in the roentgenogram may not be diagnostic, they may be of considerable value in association with the anamnesis, or the clinical history, of the patient. Aimard<sup>1</sup> has shown a mass of calcified tubercles on the lower border of the liver mistaken for gallstones. Such calcified shadows are usually not homogeneous in density or regular in outline. They may be clumped or scattered throughout the parenchyma. In the

latter case it may be difficult to differentiate calcification from intra-hepatic stones. Calcification may occur in the liver as a result of small abscesses, fungus infection (actinomycosis and blastomycosis), and parasitic infestation, such as echinococcus, pentastomum denticu-

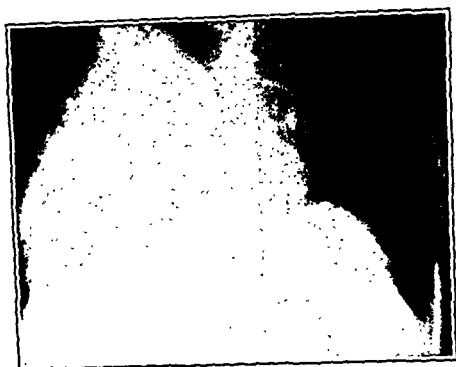


Fig. 6.—Localized bulge of left diaphragm. Due to a tumor of the liver.



Fig. 7.—Metastatic malignancy involving the liver. Lateral view shows marked enlargement with elevation of the right dome of the diaphragm.

latum, and, rarely, cysticureus, distoma, or psorospermia (Fig. 5). Multiple small calcifications may occur as a result of thrombosis associated with cavernous angiomas of the liver. A calcified plaque, the result of a perihepatitis, at times may be demonstrable in the roentgenogram.



Occasionally air and fluid levels in the liver can be shown, if the roentgenograms are made in the erect posture. If these shadows can be localized to the liver parenchyma, they usually indicate an abscess or cyst. Their presence indicates either a fistula or an infection by gas-forming organisms.

Lepennetier and Altman<sup>46</sup> have divided the supracolic hydroaerial images as follows: (1) subphrenic abscess, (2) hydatid pyopneumocysts of the liver, (3) chronic peritonitis of the hepatic flexure region or a high loop of jejunum, (4) certain forms of hepaptosis with interposition of a loop of bowel between the liver and diaphragm, and (5) images of the gastroduodenal region. Gangrenous gaseous cholecystitis is a rare condition which may produce an air-fluid level in the right upper abdomen. It may be distinguished by the presence of gaseous infiltration of the wall of the gall bladder.<sup>78</sup> Sometimes these air and fluid levels may be confused with subphrenic abscesses, as in the case reported by Altounyan,<sup>4</sup> in which a large air and fluid level was found to be due to a hydatid cyst. Gumma or other localized tumors, if near the superior surface of the liver, may cause a localized nodulation of the right dome of the diaphragm (Fig. 6). The *hepar lobatum* of syphilis may be distinguished by the smooth, nodular shadow of the enlarged viscus. In leukemia the liver may become enormous in size and sometimes hematogenous metastatic malignancy produces a gigantic liver (Fig. 7). Cystic disease of the liver is not common. It may be suspected when an enlarged liver is associated with pyelographic evidence of polycystic kidneys.

Liver abscess, with the exception of tropical abscesses, occurs most frequently as a result of infection transmitted through the portal system or bile ducts. Sérégé<sup>77</sup> has shown that there are two currents of blood in the portal vein (Fig. 8). One of these originates in the superior mesenteric vein and is distributed in the right lobe of the liver; the other, arising in the inferior mesenteric vein, finds its way chiefly to the left lobe. In our experience most liver abscesses have been associated with infection originating in the right abdomen and hence have involved the right lobe of the liver. The importance of the roentgen examination in abscess of the liver has been shown by Eliason,<sup>23</sup> Pancoast,<sup>58</sup> and Granger.<sup>33</sup> Careful fluoroscopic study and film examination are essential. In many cases serial examination from day to day is necessary before the diagnosis can be established. Pancoast<sup>58</sup> states that the roentgen evidences may not be seen before the fifth day following the onset of the abscess. Roentgen criteria of liver abscess are:

1. *Elevation of the Diaphragm.*—This may be slight or high. The contour of the diaphragm may be smooth or there may be a nodular, localized bulge. Often the costophrenic or cardiophrenic angles are clear. A sudden elevation of the right diaphragm during the course

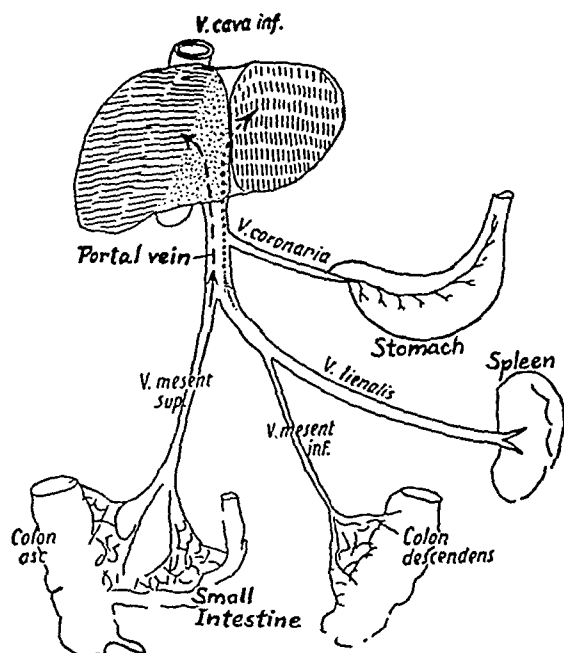


Fig. 8.—Diagram showing two currents in the portal vein. From L. Lichtwitz (Pathologie der Functionen und Regulationen, 1936) after C. Henschen.



Fig. 9.

Fig. 10.

Fig. 9.—Liver abscess. The right diaphragm is not elevated but shows some restriction of motion.

Fig. 10.—Liver abscess. Same patient as shown in Fig. 9, a few days later following rupture of the liver abscess. Right dome now elevated and fixed. There is a lumen reaction in the right lower lobe.

of a day-to-day examination may mean rupture of a liver abscess into the subphrenic region<sup>58</sup> (Figs. 9 and 10).

2. *Restriction of Motion of the Diaphragm.*—According to Pancoast,<sup>58</sup> this may occur in spite of the situation of the liver abscess. When it is adjacent to the superior surface of the diaphragm, the restriction is apt to be more pronounced than when the abscess is deeper in the liver parenchyma. This limitation of motion is not present with tumors or gumma, which may produce localized or diffuse elevation of the diaphragm. Elevation of the diaphragm, with limitation of its respiratory excursion, also may occur as the result of operative trauma.<sup>3</sup> In such cases one or both domes of the diaphragm may be affected. The condition may last only a few days, and the knowledge of a recent operation avoids diagnostic confusion. Nonsuppurative cholangitis may cause some restriction in the excursion of the diaphragm, but this usually is not associated with marked elevation. Here again, the clinical findings aid in differentiating liver abscess.

3. *Lung Reaction.*—Although this is more common in association with subphrenic abscess, it may occur with liver abscess when such a lesion is near the diaphragm. It consists of a more or less hazy increase in density involving the lower right lung field and may be associated with a pleuritis and effusion. This pulmonitis and pleuritis sometimes are quite confusing, so that in spite of careful study it is not always possible to differentiate roentgenologically between a primary infectious process below the diaphragm and one above the diaphragm. In such cases great help is afforded by removing and examining the fluid from the pleural cavity. Whereas clear fluid indicates a lesion primarily below the diaphragm, purulent fluid indicates an infectious process originating in the thorax. The roentgen localization of the abscess in the liver can be made only by finding an hydroaerial image in the film made in the erect posture. Unfortunately, this is not possible in many cases.

Abscesses of the liver may rupture Glisson's capsule into the free abdominal cavity, the pleural cavity, the lungs, bronchi, pericardium, or other structures. A subdiaphragmatic abscess, occurring as a result of rupture of a liver abscess, may cause elevation and fixation of the dome of the diaphragm. Granger<sup>23</sup> has indicated that one can differentiate a subphrenic abscess secondary to a hepatic abscess from one secondary to a peritonitis by a study of the pleurodiaphragmatic angles. In the former type he states that the cardiophrenic angle and the anterior costophrenic angle may be obliterated; whereas, in the latter the lateral costophrenic and posterior costophrenic angles are obliterated. An air-fluid level may or may not be present in subphrenic abscess.

Abscess of the left lobe of the liver is less apt to affect the diaphragm. Miles<sup>59</sup> has collected eighty-five cases of abscess of the liver.

eight of which involved the left lobe. The clinical symptoms and signs may be vague and may last for a variable period of time. Such abscesses, because of their position, tend to cause downward enlargement of the liver. The roentgen diagnosis is based upon fluoroscopic examination of the barium-filled stomach and upon film examination made in the posteroanterior and lateral positions. These studies show a downward and posterior displacement of the stomach in cases where the abscess is located laterally. When the abscess is more mesial, the posterior displacement of the fundus and cardia is less. Miles<sup>50</sup> states that when the abscess involves the caudate lobe, the distal portion of the stomach may be displaced downward and forward. In the differential diagnosis of these abscesses it is necessary to consider other tumors which occur in this position, chiefly gumma, but also echino-



Fig. 11.—Increased density of the liver and spleen. Roentgen appearance similar to that seen after injection of thorium. This was accidentally discovered in a routine roentgenogram of the abdomen. We were unable to explain this peculiar appearance and tests showed no evidence of radioactivity. No history of previous thorium injection. Satisfactory diagnosis not available. (Courtesy of Dr. Paul Bishop.)

coccus cysts, metastatic carcinoma, hemangioma, omental cysts, retroperitoneal malignancy, and pancreatic tumors or cysts.

Thorium dioxide sol has been used in the demonstration of diseases of the liver. This radio-opaque substance has an affinity for cells of the reticuloendothelial system. When injected intravenously, it causes increased density of the liver and spleen (Fig. 11). Such increase in radio-opacity depends upon the amount and distribution of the reticuloendothelial cells. We have had no experience with this procedure. In general the use of the substance has been restricted to experimental animals and patients with incurable diseases. While there is no doubt of its value as a diagnostic procedure, there are certain dangers which accompany its use. Immediate reactions may include urticaria, skin

and mucosal hemorrhages, chills, headache, diarrhea, and asthmatic attacks. Fervers<sup>25</sup> has reported death immediately following injection in the human being. Rupture of the spleen or liver may occur.<sup>17</sup> Late reactions may be the result of the radioactive properties of thorium. Pohle and Ritchie,<sup>65</sup> after studying the effects of thorotrast in rabbits, recommend restriction of its use for diagnostic purposes to incurable cases. Naegeli and Lauche<sup>54</sup> have observed degeneration adenomas in the liver five years after the injection of thorium in the dog. Such damage, however, is not in accord with all observations and may be the result of excessive dosage. Yater and others<sup>86</sup> have examined 200 patients following hepatosplenography with thorium dioxide. In the dosage used by them ( $1\frac{1}{2}$  c.c. for each pound of body weight), they have had no immediate reactions during the past three years. They have noticed no ill-effects in patients now living, some as long as four years and nine months, and they have not found any damage to liver cells by histopathologic study of 71 cases. Hepatosplenography has been utilized as follows:<sup>86</sup> (1) To determine the nature of a mass in the upper part of the abdomen; (2) to determine the presence and kind of hepatic disease; atrophic cirrhosis, hypertrophic cirrhosis, syphilis, metastatic malignancy, primary tumor, abscess, cyst, or amyloidosis; (3) to ascertain whether metastatic lesions are present in the liver if operation is contemplated for carcinoma; (4) to demonstrate rupture of the liver or spleen; (5) to determine the cause of jaundice, whether intrahepatic or due to obstruction of the common bile duct; (6) to follow the progress of hepatic or splenic disease; (7) to demonstrate whether a lesion is above or below the diaphragm; (8) to diagnose ascites; and (9) to study diseases of the spleen.

#### VARIATIONS IN POSITION AND ANOMALIES OF THE LIVER

It has been pointed out that the normal liver is not a fixed organ but, within certain limits, is freely movable in the abdominal cavity. It is held in position mainly by the inferior vena cava, the coronary and suspensory ligaments, and by the pressure of surrounding viscera. It may be easily displaced by intraperitoneal air or fluid, leaving a wide space between the diaphragm and its superior and lateral surfaces. Bürger<sup>16</sup> has observed ten cases of partial dystopia of the liver in which there was an interposition of portions of the intestinal tract between the liver and the diaphragm or lateral abdominal wall. Distention of these loops by gas may cause pain, radiating to the back and right shoulder. In all the cases which Bürger observed, there was a stenosing parapyloric ulcer, which may have accounted for the downward and medial displacement of the liver. One of us<sup>87</sup> has previously called attention to interposition of gas shadows between the liver and the diaphragm, secondary to a complete dislocation of

the liver. In this case the haustral markings of the colon could be identified in the roentgenogram. The condition also may be the result of eventration of the right diaphragm<sup>64</sup> or a right phrenic paralysis.<sup>70</sup> The surgical importance of this condition can be seen illustrated in Fig. 12. Following a subtotal gastrectomy for duodenal ulcer, this patient was examined because of a suspected subdiaphragmatic abscess. The films show air and fluid levels lateral to and above the right lobe of the liver. With this evidence, a needle was inserted into the parahepatic space in an attempt to corroborate the diagnosis. A transdiaphragmatic approach then drained the abscess. At autopsy the condition proved to be an interposition of multiple loops of jejunum with a localized peritonitis and subphrenic abscess.



Fig. 12.—Hepatositis and subphrenic abscess. Air and fluid levels represent collections in the jejunum above and lateral to the liver. (Courtesy of Dr. Karl Kornblum.)

Congenital anomalies of the liver are not common. Complete situs transversus is not difficult to diagnose in the roentgenogram, if one looks for it. Transverse furrows may sometimes be identified by the uneven appearance of the right dome of the diaphragm. Riedel's lobe may be readily demonstrable in the properly exposed roentgenogram, but it may be missed if careful roentgen technique is not carried out or if the individual be muscular or obese. Multiple lobulations, isolated accessory lobes, or attachment of the left lobe to the spleen is usually not shown in the routine roentgenogram of the abdomen.

Anomalies in size of the liver may occur as a diminution in the right or left lobe or as an increase in the size of any of the four lobes. We

have had the opportunity to observe one case of anomalous enlargement of the right lobe of the liver.<sup>44</sup> In the lateral roentgenogram of the chest and diaphragm the shadow of the enlarged liver, superimposed on the cardiac shadow, produced an image which was mistaken for an interlobar collection of fluid between the right middle and lower lobes (Figs. 13 and 14). At autopsy, a huge right lobe of the liver had elevated the diaphragm to the level of the second anterior interspace.

#### THE GALL BLADDER

The function of the gall bladder is to receive, store, and concentrate bile delivered to it through the biliary system from the liver cells. It also may equalize the pressure in the biliary system and periodically



Fig. 13.—Anomalous enlargement of the right lobe of the liver. In the lateral view the appearance simulates an interlobar collection of fluid. (Case previously reported by Dr. Kornblum and Dr. Stephenson, *Am. J. Roentgenol.* 23: 35, 1930.)

deliver bile into the duodenum.<sup>55</sup> The principal physiologic properties of the gall bladder are absorption, secretion, and motor activity. By virtue of these properties, Graham and Cole<sup>30, 31</sup> developed a roentgenographic test of gall-bladder function. In 1924 they produced successful roentgenograms of the gall bladder by the use of sodium or calcium salts of tetraiodophenolphthalein and tetrabromphenolphthalein. Ivy,<sup>39</sup> Ravdin and co-workers,<sup>67</sup> and others have shown that the gall bladder may concentrate hepatic bile as much as six to seventeen times. This concentration depends upon the absorption of water from the gall-bladder contents. When absorption occurs, it creates sufficient concentration of the sodium tetraiodophenolphthalein to permit visualization of the gall-bladder shadow in the roentgenogram. Failure to

see the gall bladder after the proper administration of sodium tetraiodophenolphthalein may be due to: (1) damage to the gall-bladder wall, (2) inability of the liver cells to excrete the dye, (3) obstruction of the cystic duct, (4) incompetency of the mechanism of the sphincter of Oddi, and (5) certain conditions which may be present outside of the biliary tract and which may interfere with the absorption, secretion, or concentration of the dye.

Indications for this test are obvious. While it is primarily a demonstration of functional activity, it is, also, of great value in the determination of any anatomic deformity. Contraindications to the method are few. Graham and others<sup>32</sup> mention cardiac decompensation and threatened uremia as contraindications to the injection of sodium tetraiodophenolphthalein. We have not hesitated to use it orally in such conditions. Although we do not advocate the promiscuous use

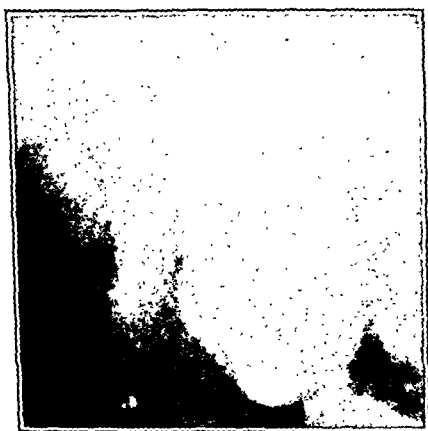


Fig. 14.—Deformed gall bladder, due to pressure from an enlarged liver.

of the drug in patients with severe liver damage or with obstruction of the common duct, we do not believe that such are definite contraindications in all cases. The use of the procedure is limited in obstructive jaundice because: (1) the examination has not proved of value in demonstrating the gall bladder, (2) the use of the drug may cause pancreatitis, when there is an obstruction in the common duct near the duodenum, and (3) further damage to already damaged or impaired liver cells may occur.<sup>69</sup> Rudisill,<sup>72</sup> however, has demonstrated the gall bladder roentgenographically in seven of eight cases of catarrhal jaundice and we have made at least one similar observation.

Iodism or allergic reactions are uncommon following the use of sodium tetraiodophenolphthalein. Reactions to the intravenous injection also are uncommon but may be more severe than when the dye is given orally. Following injection, the patient may complain of nausea, vomiting, chills, circulatory depression, fever, and abdominal cramps of varying degrees of intensity.<sup>21</sup> Orally the drug may cause



nausea, vomiting, diarrhea, and abdominal cramps of severe or mild degree. Skin reactions may occur and are usually mild.

#### TECHNIQUE OF DYE ADMINISTRATION

It is desirable to expose a film of the gall-bladder region before the sodium tetraiodophenolphthalein is given. This is routine in some laboratories, but we have not used it because: (1) many of our patients have a gastrointestinal examination or urographic studies which serve the same purpose, (2) one more day is added to the usual two-day examination.

It has been our custom to use the oral method of dye administration as a routine procedure. Occasionally, when vomiting is severe or pyloric stenosis is present, we give the dye by intravenous injection. Sandström,<sup>74</sup> in 1931, and Stewart and Illick,<sup>81</sup> in 1935, advised fractionating and increasing the peroral dosage on the basis that this procedure produces a cumulative effect in the contrast filling of the gall bladder. We have used a modification of the intensified technique outlined by Golden.<sup>28</sup> Briefly this consists of the ingestion of 60 gr. of pure sodium tetraiodophenolphthalein immediately after a "low fat" noonday meal, the day previous to the roentgen examination. This dose is repeated on the same day following a similar evening meal. The patient reports to the department the next morning, twenty-one hours after the first—14 hours after the second—dose of the dye has been taken. We make no effort to administer excessive carbohydrate, other than that which the patient may receive as the result of the low fat meals. Total abstinence from food or water is required after the last dose of the drug. One dram of tincture of opium is given one-half hour after each dose of the dye.

When the intravenous injection is preferable, we use 40 mg. of sodium tetraiodophenolphthalein per kilogram of body weight. The drug, diluted with normal saline solution, is injected by gravity, through carefully sterilized glassware and tubing. The injection is given the evening before the film examination and the patient is kept on a fasting diet in the interim. Certain writers<sup>83</sup> have pointed out that it is possible to make simultaneous tests of liver function by the use of the intravenous method of giving the dye.

Other methods of administering the dye have been used. A rapid method of cholecystography has been outlined by Antonucci.<sup>6</sup> By first placing the patient on a low carbohydrate diet for a few days and then injecting 125 c.c. of 40 per cent glucose solution immediately preceding the injection of 2 or 3 gm. of dye, the gall bladder may be visualized in one-half hour and reaches maximum opacity in two hours. Milani<sup>49</sup> states that one can differentiate the normal gall bladder from the strawberry gall bladder by this method. In the latter cases the gall bladder is not seen before two hours following the injection of the dye.

## ROENTGEN TECHNIQUE

The first film made is a large one (14 by 17) to include the entire abdomen. We have found this extremely useful in diagnosing many abdominal conditions which otherwise would be missed. The film is intended to locate the gall bladder and to determine the size of the liver. In addition we have found diaphragmatic hernia, calcified abdominal aneurysms, calcified lymph nodes, calcified adrenals, cold abscess, subphrenic abscess, calcifications in the kidneys, calcifications in the spleen and liver, myocardial aneurysm, and situs transversus. Our second film (10 by 12) is exposed immediately after the first and is centered over the gall-bladder region with the patient slightly rotated (20 to 30°), so that the right side is away from the examining table. These two films are developed at once and viewed. If they are satisfactory, the fatty meal is given without delay; otherwise, more films are exposed as indicated. We have found the use of pitressin valuable in eliminating gas shadows and contents in the hepatic flexure which interfere with visualization of the gall bladder. A cleansing enema also can be used for this purpose. The last film is made one-half hour after the fatty meal has been eaten. Under some circumstances, such as lack of gall-bladder contraction, more films may be exposed to determine the approximate emptying time of the gall bladder.

## NOMENCLATURE AND INTERPRETATION OF ROENTGENOGRAMS

In 1935 one of us<sup>60</sup> pointed out that the radiologist has no right to make a diagnosis of normal functioning or nonfunctioning gall bladder from the roentgenograms and therefore offered the following nomenclature for reporting the results of cholecystographic studies.

A. *Functioning Gall Bladder*.—Such an interpretation would include those gall bladders which showed good concentration of the dye and good emptying after the fatty meal.

1. *Functioning gall bladder with stones*: Such an interpretation would include those gall bladders which showed good concentration and good emptying, but in which stones could be identified.

2. *Functioning gall bladder with mural growth (papilloma)*: Such an interpretation would include those gall bladders with good concentration and emptying but in which, after changing position, the filling defect remained constantly in the same location.

3. *Functioning gall bladder with adhesions*: Such an interpretation would include gall bladders that showed good concentration and emptying but which, due to their peculiar contour or location, indicated pericolic adhesions. This diagnosis is difficult but is included to make the classification complete.

4. *Functioning gall bladder with anomalies*.

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It is desirable to expose a film of the gall-bladder region before the sodium tetraiodophenolphthalein is given. This is routine in some laboratories, but we have not used it because: (1) many of our patients have a gastrointestinal examination or urographic studies which serve the same purpose, (2) one more day is added to the usual two-day examination.

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shaped gall bladders which at operation were bound down or deformed by extensive pericholecystic fibrous changes. Fig. 14 shows a deformity which is due to pressure from an enlarged liver.



Fig. 15.—Opaque gallstones. The faint shadow of a partially functioning gall bladder can be seen.



Fig. 16.—Irregular calcification in cold abscess. Gall-bladder shadow can be seen above the cold abscess.

*Calculus Cholecystitis.*—The roentgenographic shadow cast by an opaque gallstone depends not only on its total calcium contents but particularly on the distribution of the calcium in the stone.<sup>70</sup> It is probably true that less than one-third of all gallstones are radio-opaque (Fig. 15). A discussion of the etiology of gallstones will be avoided,

*B. Partially Functioning Gall Bladder.*—Such an interpretation would include those gall bladders which did not show adequate dye concentration or ability to empty properly, or which became larger after the fatty meal.

1. *Partially functioning gall bladder with stones:* Such an interpretation would include those gall bladders which did not show adequate dye concentration or emptying and in which gallstones could be identified.

2. *Partially functioning gall bladder with anomalies.*

*C. Abnormally Functioning Gall Bladder.*—Such an interpretation would include those cases in which there was very poor or no gall-bladder visualization or those in which the gall bladder increased in size during the examination, thereby indicating a reversal of flow.

1. *Abnormally functioning gall bladder with stones:* Such an interpretation would include those cases in which there was very poor or no gall-bladder visualization, but in which opaque calculi could be seen. Stones could be classified as "nonopaque" and "opaque."

2. *Milk of calcium bile.*

3. *Calcified gall bladder.*

4. *Abnormally functioning gall bladder with anomalies.*

*Noncalculous Cholecystitis.*—This disease may produce a dense, faint, or absent gall-bladder shadow in the cholecystogram. The density of the dye shadow varies with the amount of damage to the gall-bladder wall.<sup>20, 30</sup> The function of the gall bladder may return to normal, as indicated by cholecystography, following major or minor inflammatory changes to its wall.<sup>27, 40</sup> This may account for the fact that the pathologically abnormal gall bladder has shown what we would term "functioning gallbladder," by the cholecystographic test. Hodges and Lampe<sup>37</sup> encountered a 16 per cent error in this respect. They have also noted that among twenty-one patients with proved major inflammatory disease of the gall bladder, 95 per cent showed faint visualization or no shadow in the roentgenogram. Whether the pathologic evidence or the roentgen evidence is the proper criteria in relation to the clinical symptoms is undecided. Suffice to say that a fairly large percentage of patients who have had a cholecystectomy for noncalculous cholecystitis are not relieved of their symptoms. Ravdin<sup>68</sup> put this even more forcefully when he stated: "It is very likely that in well over half of the operated cases, the gallbladder does not account for the patient's symptoms."

*Adhesions.*—There are some writers who try to interpret anatomic deformity or motor disturbance in terms of pericholecystic adhesions. We believe that the roentgenologist who attempts such interpretations, in many cases, is treading on thin ice. Our experience has included roentgenologically deformed gall bladders which were entirely normal and without adhesions at operation, and roentgenologically normally

shaped gall bladders which at operation were bound down or deformed by extensive pericholecystic fibrous changes. Fig. 14 shows a deformity which is due to pressure from an enlarged liver.



Fig. 15.—Opaque gallstones. The faint shadow of a partially functioning gall bladder can be seen.



Fig. 16.—Irregular calcification in cold abscess. Gall-bladder shadow can be seen above the cold abscess.

*Calculous Cholecystitis.*—The roentgenographic shadow cast by an opaque gallstone depends not only on its total calcium contents but particularly on the distribution of the calcium in the stone.<sup>70</sup> It is probably true that less than one-third of all gallstones are radio-opaque (Fig. 15). A discussion of the etiology of gallstones will be avoided,

except to state that two factors may play an important role. The first of these is obstruction; the second, inflammatory changes in the gall-bladder wall.<sup>5, 35, 62</sup> Occasionally we have noticed a stone which has a layer of calcium on only one portion of its periphery. This we

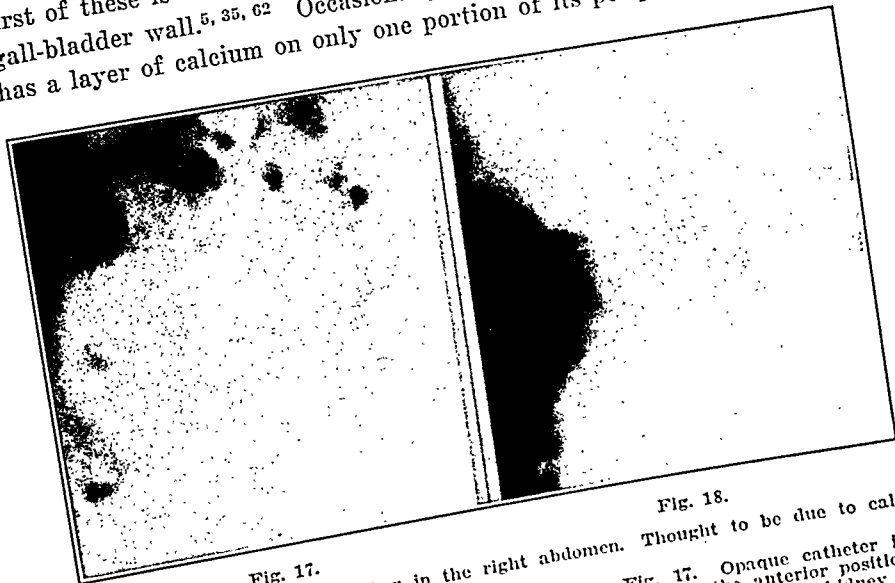


Fig. 17.

Fig. 17.—Large dense shadow in the right abdomen. Thought to be due to calculus in the gall bladder.

Fig. 18.—Lateral view, same patient as shown in Fig. 17. Opaque catheter in ureter shows the shadow to be due to a renal calculus. Note the anterior position of the calculus in relation to the spine. This sometimes occurs when the kidney is enlarged.

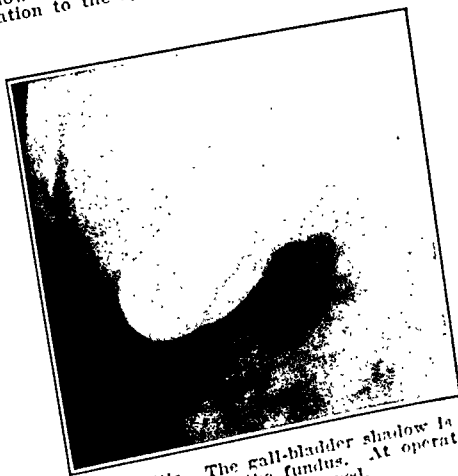


Fig. 19.—Calculus cholecystitis. The gall-bladder shadow is quite dense, but there is a single, large, nonopaque stone in the fundus. At operation, a typical "strawberry gall bladder" containing a stone was removed.

have attributed to the fact that at one time or another this stone has obstructed the cystic duct. The associated inflammatory changes in the gall bladder have resulted in the deposition of calcium on the exposed side of the calculus.

*Differential Diagnosis of Opaque Calculi in the Right Upper Abdomen.*—The most common opaque shadows in this region, which may be confused with gallstones, are: renal calculi, calcified glands or vessels, opaque shadows in the gastrointestinal tract (barium in diverticula of the colon), calcification in the liver or pancreas, and calcification in a tuberculous abscess (Fig. 16). Careful and often repeated roentgeno-



Fig. 20.—Nonopaque gallstones, developed in twenty-six months.

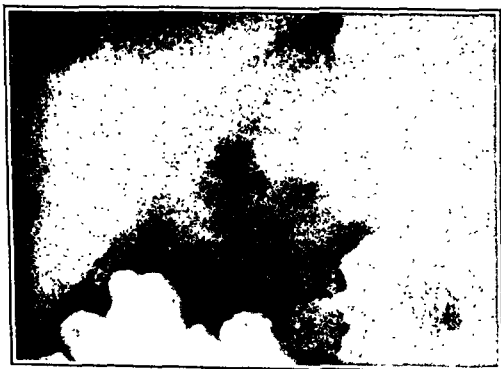


Fig. 21.—Gas shadows in the duodenum. Such shadows may be confused with nonopaque gallstones.

graphic or roentgenoscopic examinations, with the patient in various postures, frequently are necessary for correct interpretation. Pyelography may be required to exclude renal calculi (Figs. 17 and 18). Moles or small tumors on the patient's skin, particularly if they are in a position where they are pressed against the film or examining table, may produce a round, dense shadow in the roentgenogram.



Following the use of the Graham-Cole test, the gall bladder involved by calculous cholecystitis may be dense, faint, or not visualized. The detection of nonopaque stones in the roentgenogram depends upon the presence of contrast substance (Fig. 19). Fig. 20 shows multiple nonopaque stones which have developed in a period of twenty-six months. Nonopaque stones may be confused with gas in the intestine (Fig. 21). Akerlund<sup>2</sup> and others have demonstrated stratification or layers of bile in films made in the erect posture. In five of Akerlund's cases nonopaque stones could be demonstrated as filling defect between the layers of different density. Kirklin<sup>42</sup> was able to diagnose gallstones as such in 70.8 per cent of the cases examined. He found, however, that in a group of 415 patients having gallstones at operation, 99 per cent showed abnormal cholecystographic findings. Our own observations have led us to an absolute diagnosis of stones in only 27 per cent of patients in whom stones were found at operation. We have been inclined toward conservatism in this respect, because we feel that the danger seems to be in interpreting too much, rather than not enough, in patients with abnormal gall-bladder function. Hodges and Lampe<sup>37</sup> have summarized the situation in their study of 121 cases of proved calculous cholecystitis.

NO. CASES		ROENTGEN DIAGNOSIS OF STONES	
88	No dye shadow	28	32%
33	Dye shadow	31	94%
121	All cases	59	49%

These investigators write: "It is noteworthy that normal visualization without stones was never reported in the case of patients later shown to harbor calculi."

A comparison of the value of cholecystography and biliary drainage in the diagnosis of gallstones has been presented by Bockus and others.<sup>10</sup> Biliary drainage was accurate in diagnosing or excluding gall-bladder pathology in 98 per cent of 148 cases; whereas, in this same group cholecystography gave an accurate diagnosis in 88.4 per cent. In cholelithiasis alone biliary drainage indicated stones in 83.2 per cent of their cases, as against 29.2 per cent by cholecystography. Biliary drainage, however, is satisfactory only when "B" bile is obtained and its efficacy in the diagnosis of stones depends upon the skill of the observer. For these reasons, the authors conclude that, if one study only is to be carried out, it should be intravenous cholecystography. Miller<sup>51</sup> has found duodenal drainage indicative of stone or lack of function in 91 per cent of stone cases, while cholecystography revealed stone or lack of function in 87 per cent of these patients.

Milk of calcium bile is a term which has been used to indicate deposits of opaque material, chiefly calcium carbonate, in the gall bladder. This condition has been adequately described by Churchman,<sup>19</sup>

Kornblum and Hall,<sup>42</sup> Phemister and others.<sup>63</sup> Prior to operation, the roentgen examination is the only means of establishing this diagnosis. Roentgen diagnosis is contingent upon the finding of a dense gall-bladder shadow, which may be homogeneous or mottled, depending upon the amount of nonopaque detritus present. The gall-bladder is sometimes small and shrunken and does not empty after the fatty meal (Fig. 22). Often, an opaque calculus can be seen in the region of the cystic duct. Films made in the erect posture may demonstrate partly calcified debris in the fundus of the gall bladder, above which there is a homogeneous shadow of lesser density (Fig. 23). When the condition is suspected, films should be exposed without the administration of gall-bladder dye.

Calcification of the gall-bladder wall or porcelain gall bladder has been described by Blatter<sup>9</sup> and others. This condition may be confused with a dye-containing viscus, milk of calcium bile, or calcified



Fig. 22.

Fig. 23.

Fig. 22.—Milk of calcium bile and nonopaque gallstones. There is no change in the size or shape after the fatty meal. Putty-like material, mixed with cholesterolin stones, was found at operation.

Fig. 23.—Milk of calcium bile. Erect film showing fluid level in the gall bladder. At operation, a thin, milky fluid was found, associated with a small amount of detritus and a few small, nonopaque stones.

gallstone. It may present, however, a characteristic streaked or mottled appearance which does not vary with the position of the patient (Fig. 24).

Tumors of the gall bladder have been uncommon in our experience. Statistics indicate that primary carcinoma of the gall bladder may be found among 5 to 7 per cent of all carcinomas found at autopsy. Malignant lesions are apt to produce an early occlusion of the outlet of the gall bladder and, hence, do not lend themselves to visualization by cholecystography. Our observation concurs with that of other writers, that this most important group of tumors of the gall bladder has not been diagnosed by cholecystography, except in rare instances. They are frequently associated with gallstones, however. Wilkie<sup>65</sup> has had thirty-one cases of carcinoma of the gall bladder, all of which had associated biliary calculi.

Benign tumors of the gall bladder may be demonstrated by cholecystography. The roentgen diagnosis of these conditions has been excellently presented by Kirklin<sup>43</sup> and by Moore.<sup>53</sup> Papillomas are usually small, not exceeding 1 cm. in diameter. They may be single or multiple. Frequently the gall bladder shows no other changes, although there may be an associated chronic cholecystitis or cholelithiasis. The roentgen diagnosis depends upon the finding of one (or more) clear, oval, or circular defect which remains constant with changes in the position of the patient (Fig. 25). Such a defect will always be adjacent to the gall-bladder wall. These shadows are most apt to be seen in those films made during evacuation of the opaque dye from the gall bladder. Not infrequently the gall-bladder shadow is denser than average. Cholesterol stones may be differentiated by

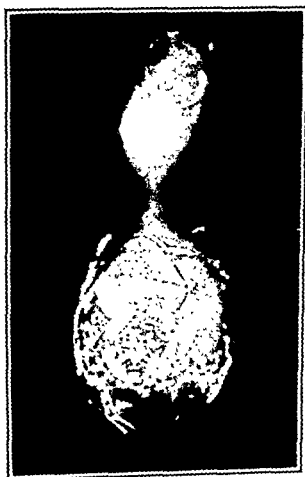


Fig. 24.



Fig. 25.

Fig. 24.—Calcification of the gall bladder. Roentgenogram made after removal shows the irregular flakes of calcification in the wall of the viscus.

Fig. 25.—Papilloma of the gall bladder. The small defect can be seen near the superior surface in the body of the gall bladder. The gall-bladder shadow is quite dense.

their tendency to change position in their relation to the gall-bladder wall, by their angular outline, or by the presence of calcium deposit.

Adenomas most often occur in the fundus of the gall bladder. They may be larger than the papillomas. The gall-bladder shadow may be dense or faint. Like the papillomas, the adenomas are more easily detected roentgenologically in films made during the emptying phase of the gall-bladder function.

#### EMPTYING OF THE GALL BLADDER

Many investigators have shown that the gall bladder contracts, in response to certain stimuli, to empty its contents into the cystic and common ducts. As yet there is no agreement among radiologists as

to the optimum time for the normal gall bladder to empty itself. Variations occur with age and sex, as can be seen from the following results of Boyden and Fuller<sup>12</sup> and Boyden and Grantham.<sup>13</sup> Before puberty, boys show more rapid emptying than girls. After puberty, females show more rapid emptying than males. In old age women evacuate 81 per cent of the contents in thirty minutes; men, 65 per cent. There is very little difference in emptying time between female children and adult women. Boys, however, show much more rapid evacuation than adult males. Because of such variation, roentgenologists would do well to pay less attention to complete emptying as an important point in diagnosis. It is important to determine, however, whether the gall-bladder shadow (1) diminishes in size, (2) remains unchanged in size, or (3) increases in size.

Failure of the gall bladder to diminish in size after the proper technique has been used may be due to a number of conditions; such as mechanical kinking of the cystic duct, ball valve obstruction of the cystic duct, milk of calcium bile with or without a cystic duct stone, spasm of the sphincter of Oddi mechanism, anomalies, adhesions, and reflex phenomena from lesions outside the biliary tract. Increase in the size of the gall-bladder shadow occasionally may be seen. An explanation of this occurrence may be found in the work of Ravdin and others,<sup>67</sup> who found that in dogs water could flow out of or into the lumen of the gall bladder. Practically all of these conditions which interfere with the emptying of the gall bladder, or even increase its size, have been rather loosely grouped together under the term "dyskinesia of the gallbladder." Further investigation is necessary to evaluate the meaning of this disturbance in function. For the present we are inclined to classify gall bladders which may show good or faint visualization after dye, yet which do not show proper dynamics after the fatty meal, as "partially functioning."

#### ANOMALIES OF THE GALL BLADDER

Congenital absence of the gall bladder is rare. Bower<sup>11</sup> was able to find 59 cases in the literature up to 1928, when he added 1 of his own. Gross,<sup>34</sup> in a more recent review, found a total of 73 cases of absence of the gall bladder and 28 recorded cases of double gall bladder. He states that the accessory gall bladder may be contiguous with the normal organ, under the left lobe of the liver, within the liver parenchyma, or in the gastrohepatic omentum. Boyden<sup>14</sup> is of the opinion that accessory gall bladder occurs in about 1 of every 3,000 or 4,000 human beings. He classifies this anomaly as: (1) *vesica divisa* or bilateral gall bladder, and (2) *vesica duplex*, either Y-shaped with two cystic ducts merged into one, or *ductula*, with two complex cystic ducts opening separately into the common duct.

A diverticulum of the gall bladder may occur along the free surface of the organ or even on the hepatic surface, anywhere between the neck and the tip of the fundus.<sup>34, 82</sup> Probably the most common congenital anomaly which can be demonstrated roentgenographically is the folded fundus. This has been described by Boyden,<sup>15</sup> who found that 18 per cent of a group of 165 individuals exhibited marked kinking of the gall bladder either between the body and infundibulum or between the body and the fundus (Fig. 26). The former group, he believes, represents merely an accentuation or a minor variation from the normal, which may be due to extreme modeling of the fossa vesicae felleae. The second group, which has been termed "phrygian cap," is characterized by a fixed, folded fundus. This condition, in itself, may be of no clinical significance, but it is important because it may

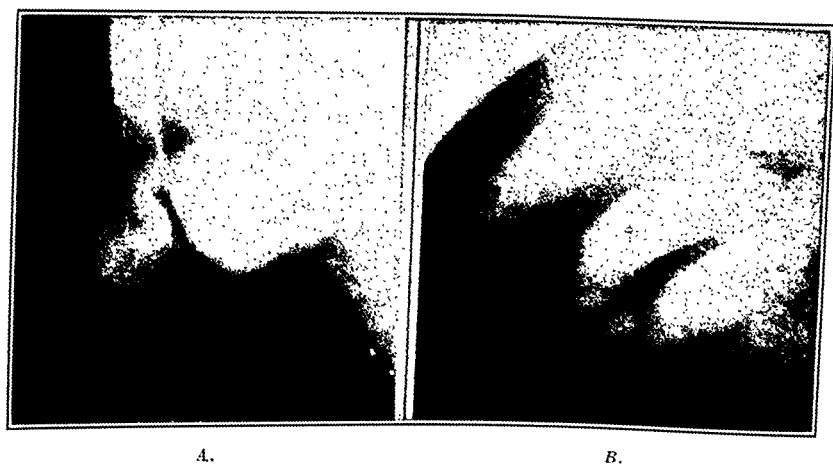


Fig. 26.—Types of folded fundus. A, Fold between the body and the infundibulum, B, "Phrygian cap."

be confused roentgenographically with double gall bladder or with diverticulum of the gall bladder.

Anomalies in position of the gall bladder sometimes may be demonstrated by cholecystography. Gross<sup>34</sup> states that a normally formed gall bladder may be found within the liver substance, under the left lobe, posteriorly under the right lobe, in the transverse fissure of the liver, or "floating" in the mesentery. The last named position may be important because of the tendency for twisting of the suspensory attachments, which might result in infarction and gangrene of the gall bladder. The intrahepatic gall bladder<sup>48</sup> is important because it may be completely missed at operation. This condition is impossible to diagnose preoperatively, except by cholecystography. The intrahepatic gall bladder is higher than normal and maintains its position in relation to the liver shadow. Its lower limit may be on a level with, or

above, the inferior edge of the liver. Often posteroanterior, oblique, and lateral roentgenographic exposures are necessary to demonstrate the true condition.

Our experience with the roentgen diagnosis of gall-bladder disease in children has been limited. In a series of 226 cases of gall-bladder disease in children under the age of 15 years, collected by Potter,<sup>66</sup> 140 had calculi; 59, cholecystitis; and 2, primary malignancy of the gall bladder. It is a well-known fact that the clinical symptoms of gall-bladder disease in children may resemble the symptoms of appendicitis and may be accompanied by it. There is also good evidence to indicate that peritoneal irritation interferes with the emptying of the gall bladder.<sup>57</sup> This may account, in part, for the relationship which has been mentioned. In the nonacute cases a cholecystogram, as well as an examination of the stomach and small intestines, may be of definite value in the diagnosis.

Sources of error associated with cholecystography by the oral method may be divided into (1) errors in technique and (2) errors in interpretation. The sodium tetraiodophenolphthalein should be kept in dark, air-tight bottles, so that oxidation does not occur. Instructions, written in detail, must be given to the patient. The roentgenograms must be of diagnostic quality and should be made with the shortest possible exposure time to prevent motion.

We insist upon visualization of dye in the bowel before rendering an opinion of an "abnormally functioning gall bladder." In this way we can be certain that the patient has ingested the dye and that vomiting or diarrhea has not interfered with its absorption from the gastrointestinal tract. Anzilotti<sup>7</sup> states that certain diseases outside the biliary tract which may produce nonvisualization of the gall bladder are pyloric and duodenal ulcers, pancreatitis, appendicitis, hyperthyroidism, diabetes, cancer, and some infections. Maun<sup>47</sup> has demonstrated pregnancy as a cause of nonvisualization. We have observed variable results in the test in patients with cardiac disease. Gibbon and Cooper<sup>27</sup> found that about 80 per cent of a group of 81 uncontrolled diabetics gave faint shadows or no visualization of the gall bladder by cholecystography. There is some evidence<sup>64</sup> to show that gall-bladder visualization and emptying may occur earlier in patients with uncontrolled diabetes. It may be necessary to arrange the technique accordingly in this group of individuals. Good and Kirklin<sup>29</sup> do not consider that extrabiliary conditions affect the function of the gall bladder. They studied 167 proved cases who showed abnormally functioning gall bladders associated with extrabiliary disease and the cholecystographic findings were accurate in 98.1 per cent.

Cholecystography is an accurate but not infallible means of detecting disease of the biliary tract. One can readily appreciate that it

A diverticulum of the gall bladder may occur along the free surface of the organ or even on the hepatic surface, anywhere between the neck and the tip of the fundus.<sup>34, 82</sup> Probably the most common congenital anomaly which can be demonstrated roentgenographically is the folded fundus. This has been described by Boyden,<sup>15</sup> who found that 18 per cent of a group of 165 individuals exhibited marked kinking of the gall bladder either between the body and infundibulum or between the body and the fundus (Fig. 26). The former group, he believes, represents merely an accentuation or a minor variation from the normal, which may be due to extreme modeling of the fossa vesicae felleae. The second group, which has been termed "phrygian cap," is characterized by a fixed, folded fundus. This condition, in itself, may be of no clinical significance, but it is important because it may

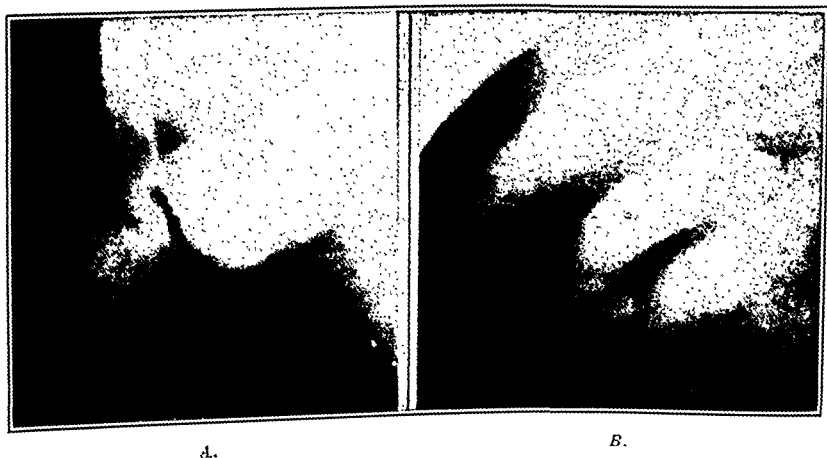


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for the cause of the obstruction. After this procedure is completed, a T-tube or catheter is inserted, hippuran again injected, and a second film exposed. The surgeon is then able to determine whether or not the obstruction has been removed.

Delayed cholangiography consists in the roentgen demonstration of opaque material injected through a catheter, tube, or biliary fistula at some time after operation, before the drainage tract is allowed to close. The procedure is quite simple. We have injected lipiodol, or equal parts of lipiodol and olive oil, under fluoroscopic guidance in many of these patients (Figs. 27 and 28). Films are exposed at intervals, depending upon the indications. The necessity for roentgenoscopic control cannot be overestimated, for it may prevent untoward reactions due to overdistention or may reveal stones or spasm which are not apparent in the roentgenogram. Hufford<sup>35</sup> has pointed out

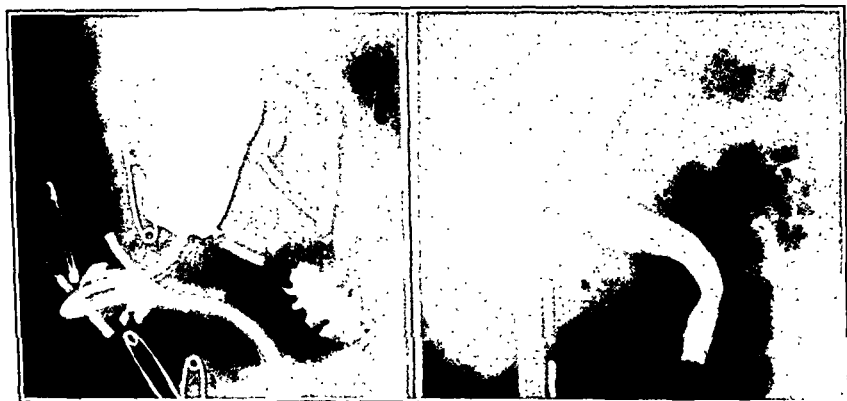


Fig. 27.

Fig. 28.

Fig. 27.—Cholangiogram. We have considered this as a normal appearance. The cholecystostomy tube, gall bladder, cystic duct, common duct, and duodenum can be identified. Note that none of the opaque oil has passed up into the hepatic ducts.

Fig. 28.—Cholangiogram. The concave filling defect which obstructs the common duct is due to a nonopaque stone. Note the dilated common duct and hepatic ducts. The opaque oil outlines many of the smaller radicles which are widely dilated.

the value of the procedure as a complementary method in determining the proper time to allow closure of the operative wound. Hicken and others<sup>36</sup> also have showed the advantage of cholangiography. The procedure is practically harmless and may provide a great deal of assurance to the surgeon and to the patient soon after operations on the biliary tract.

#### SUMMARY

We have attempted to point out the value of roentgenographic diagnosis of surgical diseases of the biliary tract. Close cooperation between the surgeon and the radiologist will afford opportunity for early diagnosis, prompt treatment, and better results.



is not a procedure to be used injudiciously, without proper regard for the many conditions which may affect the correct interpretation of results. If one may utilize the statistics of Kirklin<sup>42</sup> as an index, the general accuracy of this type of examination is about 90 to 95 per cent. This does not include cases studied after operations on the biliary tract. The value of cholecystography after cholecystostomy has not been definitely determined. This is indicated by the following table.

AUTHOR	NO. CASES REPORTED	PER CENT SHOWING FUNCTIONING GALL BLADDER
Spurling and Whitaker <sup>50</sup>	12	0
Fleming <sup>26</sup>	36	2.7
Saint <sup>73</sup>	18	38.9
Jenkinson and Foley <sup>40</sup>	28	68.0
Eliason and Ferguson <sup>22</sup>	28	21.4

Enough data are not yet available for us to determine the value of cholecystography in these patients, particularly in those individuals who may show clinical evidence of recurrence of gall-bladder symptoms, yet have a functioning gall bladder by cholecystography.

#### CHOLANGIOGRAPHY AND CHOLANGIOSCOPY

A small collection of barium in the second portion of the duodenum is sometimes noted during the course of roentgenologic examination of the gastrointestinal tract. This represents the ampulla of Vater and may be confused with a small diverticulum in this region. Retrograde visualization of the biliary tract during the course of a gastrointestinal examination is less common. Such may occur, however, if there is an obstruction in the duodenum distal to the ampulla which causes it to dilate or if there is, as a result of disease or operation, a fistula between the intestinal and biliary tract. Since 1927, methods have been devised for the direct visualization of the biliary tract following the injection of opaque media. The procedure is of value in demonstrating obstruction, in outlining stones, strictures, or fistulas, and in delineating dilatation of the biliary system. Occasionally the injection may help to flush out small stones or debris which are producing symptoms. Two methods are available: (1) immediate cholangiography, done at the time of operation; and (2) delayed cholangiography. The first method has been described by Robins and Hermanson.<sup>71</sup> When the abdomen is opened, the radio-opaque substance (hippuran) is injected through the common duct before the gall bladder is disturbed and films are exposed immediately. If the duct is patent, incision and exploration are unnecessary. If the films show evidence of obstruction, the common duct is opened and explored

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## THE ANATOMY OF GALL-BLADDER INCISIONS

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A SURGICAL incision for the exposure of the biliary passages should satisfy two requirements: adequate access to the structures sought, and absence of postoperative disability due to the incision itself. Unsightly scars are distressing to the patient and to the operator. Postoperative weakness of the abdominal wall may be due either to a partial paralysis of a rectus muscle or to a diastasis of the rectus muscles.

Vertical incisions through the substance of the rectus muscle do not seem to cause disability. This is apparently due to the scarring of the muscle to the rectus sheath which, in effect, creates an additional, diffuse, tendinous inscription. This statement is made from an experience with dissected rectus scars in the lower half of the abdomen. (In the last ten years, with a material consisting of about 1,800 cadavers, I do not recall a single scar of a gall bladder incision.) It would seem that any postoperative disability of the rectus muscle is due to an injury to its motor nerve supply. Experience with diastasis of the rectus muscles in the lower part of the abdomen gives no indication that the separation is the result of any anatomic peculiarity. Can it be that the postoperative diastasis in the upper part of the abdomen is due to the difficulty of securing sutures effectively in the loosely imbricated fibers of the sheath?

In order to present anatomic factors which may merit consideration in planning an incisional technique, the relations of the area will be summarized under the following headings:

- I. The anatomy of the skin and subcutaneous tissue as related to incisions.
- II. The composition of the rectus sheath.
- III. The course of the nerves to the rectus muscle.

### I. THE ANATOMY OF THE SKIN AND SUBCUTANEOUS TISSUE AS RELATED TO INCISIONS

In 1861 Langer, on the basis of earlier observations of Dupuytren, Malgaigne, and others, worked out the directions of the principal fiber patterns in the adult human skin by puncturing the skin with an awl. In general, a round awllike instrument thrust into the skin, by separating the principal fiber bundles, produces a slitlike opening. Upon withdrawing the awl every normal movement of the body tends to keep the slit edges in approximation. A skin incision made to coincide with the direction of the fibers also tends to close. An incision made at right

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## II. THE COMPOSITION OF THE RECTUS SHEATH

For our present purposes the rectus muscle in the upper part of the abdomen may be considered surrounded by two aponeurotic laminae derived from the internal oblique muscle. These reunite at the linea alba. In this manner a flat capsular aponeurotic sheath is formed. The muscle is firmly attached to this sheath at the several, irregularly transverse, tendinous inscriptions.

In the upper part of the abdomen there is always aponeurosis in front of, and behind, the rectus muscle. The superficial lamina of this sheath



Fig. 2.—Dissection to show the nerve supply and the sheath of the rectus muscle. The continuation of the fleshy fibers of the transversus abdominis muscle behind the aponeurotic sheath may be confusing in well-muscled individuals.

is joined and reinforced by the aponeurosis of the external oblique muscle. This layer remains muscular until it is well over the rectus. Similarly underlying the deep lamina of the sheath is the transversus abdominis muscle which likewise does not become aponeurotic in this region until well under the middle of the rectus muscle. As a result, flat muscle is found both in front of and behind the aponeurotic rectus sheath in the upper part of the abdomen at the outer margin of the rectus muscle. These flat muscle layers many times are thin and pass unnoticed. In muscular individuals these muscle layers may be very prom-

angles to the split-pattern gapes with every movement. I have shown that the subcutaneous tissues have the same cleavages as the true skin. Kocher correlated these skin cleavages with surgical incisions. Fig. 1, made from a new preparation, shows the skin cleavages in the upper part of the abdomen. Obviously, it would be difficult always to make the initial skin incision for exposure of the biliary passages to coincide completely with this pattern. Although an incision at right angles to the cleavages would result in a wound more adapted to maintain drainage,

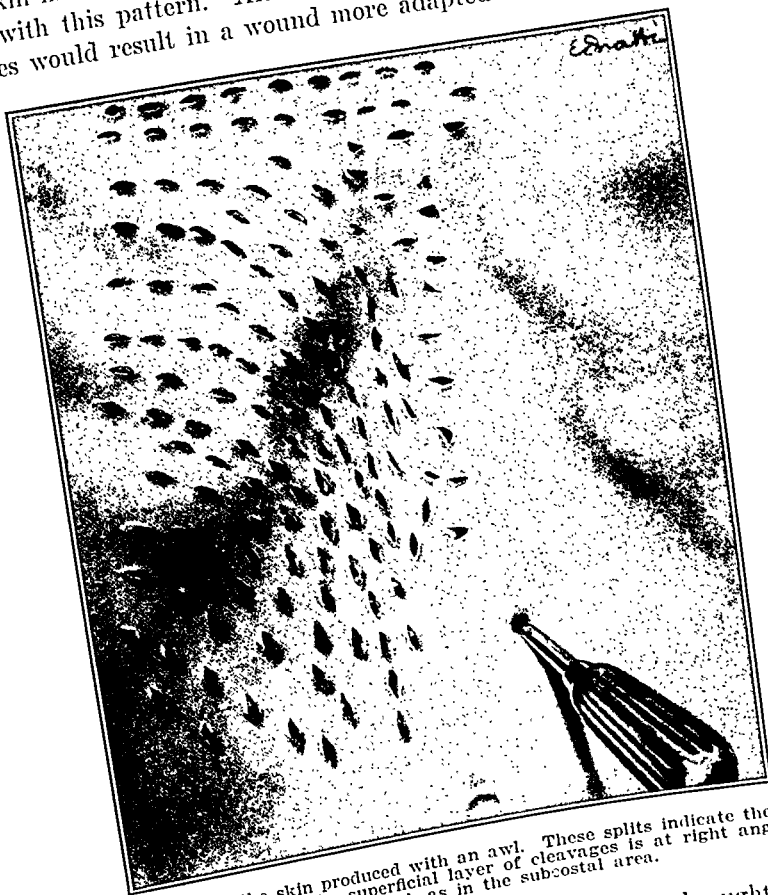


FIG. 1.—Splits in the skin produced with an awl. These splits indicate the principal fiber directions. Note that the superficial layer of cleavages is at right angles to the deep layer in a number of places, such as in the subcostal area.

in view of the end result, the drain should probably be brought through that part of the original incision, or through a stab incision which coincides with the direction of splitting.

It is neither necessary to remember the cleavage patterns nor to have a chart at hand. Thumb and finger will readily determine the directions of elasticity and rigidity of the skin. The splits run in the direction of the inelasticity and hence incisions are preferably made in this direction. This method permits the incision to be adapted somewhat to the variations in individual anatomy.

## II. THE COMPOSITION OF THE RECTUS SHEATH

For our present purposes the rectus muscle in the upper part of the abdomen may be considered surrounded by two aponeurotic laminae derived from the internal oblique muscle. These reunite at the linea alba. In this manner a flat capsular aponeurotic sheath is formed. The muscle is firmly attached to this sheath at the several, irregularly transverse, tendinous inscriptions.

In the upper part of the abdomen there is always aponeurosis in front of, and behind, the rectus muscle. The superficial lamina of this sheath



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inent, especially the inner one, the transversus abdominus muscle. Judging from frequent questions, this relationship is sometimes not sufficiently emphasized (Fig. 2).

### III. THE COURSE OF THE NERVES TO THE RECTUS MUSCLE

The essential facts of the innervation of the rectus muscle are briefly stated. The muscle receives motor branches from the lower five or six intercostal nerves. As with other muscles receiving multiple segmental innervation, anatomic studies and clinical experience show much overlapping in the terminal arborization of nerves from adjacent segments. Especially in the upper part of the rectus muscle, injury of one intercostal nerve is not accompanied by a disabling paralysis. In the gall bladder area there are encountered the seventh, eighth, ninth and tenth intercostal nerves. The arrangement of nerves found in an adult white male cadaver (Fig. 2) may be taken as typical. Variations of one segment up or down in numerical origin are encountered, but the general curving course remains the same.

This indicates then that an incision through the flat muscles may be made parallel to the curving costochondral margin with comparative safety to the nerve supply of the rectus muscle. It may be necessary to cut the ninth (or eighth) nerve but, as noted above, the injury of one segment does not disable the muscle.

Upon leaving the rib margins, the nerves, with their small accompanying vessels, course between the internal oblique muscle and the transverse abdominal muscle until they pierce the deep inner lamina of the rectus sheath to enter the posterior surface of the rectus muscle near its lateral edge. This relationship seems to make unwise incisions parallel to the lateral margin of the rectus muscle. Further, caution is indicated in media retraction of the rectus muscle. Lateral retraction of the rectus muscle through a vertical sheath incision will not disturb the nerve supply. If it is desired to make a transverse cut in the rectus muscle, the points of entrance of the nerves may be visualized and avoided.

The anatomic facts which might be considered in making these incisions appear to be sufficiently at variance with one another that it is not surprising that some surgeons disregard them altogether and strive only for a wide exposure. However, an incision just under the right costochondral border gives good exposure and is anatomically the most favorable. Occasionally, due to individual variations, this incision will be too low for the best results in skin closure. An extension of the incision transversely through the rectus muscle is compatible with the nerve distribution. No objections on anatomic grounds can be raised to linea alba incisions.

## PREOPERATIVE AND POSTOPERATIVE TREATMENT IN CASES OF OBSTRUCTIVE JAUNDICE

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OBSTRUCTION of the common duct is all too frequently considered a local disease. In reality the local site of obstruction is but an initiating incident in the more important general reaction following cessation of the normal flow of bile. Correction of the consequences of common duct obstruction naturally lies in the relief of the obstruction. However, surgical procedures designed to overcome the obstruction must wait until the patient is properly prepared for operation. No longer is immediate operation considered necessary. The preparation of the patient for operation is of primary importance in the necessary readjustment of the patient to the altered physiology following the obstruction to the outflow of bile.

Following obstruction to the common duct, a train of events occurs which result in widespread changes in the individual.<sup>1</sup> When the flow of bile from the liver is stopped either partially or completely, the liver becomes altered morphologically and physiologically, and the digestive processes become embarrassed. While the latter variation from normal is of consequence, the results of suppression of biliary outflow become of paramount importance in relation to liver function. Shortly following obstruction of the common duct, the liver becomes damaged, and it is for this reason that the patient presents a problem requiring careful study and preparation before operation is considered. This fact was well brought out by a symposium on obstructive jaundice by leading German surgeons,<sup>2</sup> where varying viewpoints were expressed regarding types of operative procedures, of the rôle of infection, and methods of treatment, but the one accepted fact was that damage to the liver parenchyma was the most important result of the obstruction. The concept that disordered liver function is the underlying defect associated with common duct obstruction has been widely accepted within the past decade.

The methods for evaluating liver function have been recently discussed by Snell<sup>3</sup> and Newman.<sup>4</sup> It is noteworthy that none of these tests has been completely trustworthy in depicting the status of the activity of the liver parenchyma. Newman<sup>4</sup> has pointed out that, since there are many functions of the liver, no one of the tests may be depended upon to tell us the whole story of hepatic insufficiency. Many of the functions of the liver are also carried on elsewhere in the body or are influenced by other organs. The relation of the liver to sugar metabolism is well known; yet this important function is greatly influenced by pancreatic and adrenal activity.

The measure of the elaboration of bile salts should afford a good criterion for liver function, but as yet we have no method for determining bile salt formation in the liver of intact patients. So far as we know, bile salts are formed solely in the liver.<sup>5</sup> This is corroborated by the fact that fetal bile has little or no bile salts present, indicating that this important hepatic function appears after the liver becomes more active when the offspring assumes independence from the maternal metabolic processes. An additional corroborative fact is the early loss of bile salts from the bile after obstruction of the common duct and the rather tardy return after release of the obstruction.<sup>6, 7, 8</sup>

In a series of cases Ravdin, Johnston, Riegel, and Wright<sup>7</sup> studied the return of bile salts in the bile following release of a complete obstruction of the common duct, and the earliest date when traces of bile salts could be found was seven days.

The care of the jaundiced patient must at all times be directed toward conserving the function of the liver under adverse conditions. It is for this reason that morphine should be used sparingly in the control of pain in these cases. In addition to the effect of morphine on the storage and mobilization of glycogen, it must be remembered that this drug is a respiratory depressant. Goldschmidt, Ravdin, and Lucké<sup>9</sup> have recently shown the effects of relative anoxic conditions on the ability of the liver to withstand the assault of anesthetics.

Recently Butsch, McGowan, and Walters<sup>10</sup> have condemned the use of morphine in controlling the pain associated with obstruction of the common duct on the ground that morphine increases intraductal tension, and therefore should increase rather than decrease pain. For many years it has been common practice to give morphine in common duct obstruction with excellent results as regards the control of pain. Morphine has an analgesic action which is capable of controlling pain even though the tension within the duct may be increased. The chief fault with morphine lies in its effect on the liver and is not concerned with its effectiveness in the control of pain. Butsch, McGowan, and Walters suggest the use of the nitrite series for control of stone colic; these drugs have a much more rational basis than morphine but are, as a rule, more fleeting in their action.

Frequently the pain associated with common duct obstruction can be controlled by bed rest and restriction of intake by mouth of food and fluid. During this period the patient should receive adequate glucose and saline solution by vein. This method assures the introduction of needed fluids and glucose and is not associated with the difficulties associated with the subcutaneous method. The rectal administration of glucose has been shown by Ebeling,<sup>11, 12</sup> Scott and Zweighaft,<sup>13</sup> Pressman,<sup>14</sup> and McNealy and Willems<sup>15</sup> to be quite ineffective. After

the period of acute colic has passed, the patient should be given a high carbohydrate diet supplemented by slow intravenous infusion of 10 per cent glucose in distilled water. By this latter means it is possible to introduce 100 to 300 gm. of glucose daily in addition to the carbohydrate taken by mouth.

The value of high carbohydrate intake in cases of jaundice from common duct obstruction has been stressed recently by Ravdin, Riegel, and Morrison.<sup>16, 17</sup> It was Ravdin and his associates, who in 1930 pointed out the beneficial effects of glucose in obstructive jaundice and indicated that the beneficial effects were associated with a partial restoration of glycogen reserve. In 1915 Opie and Alford<sup>18</sup> and Graham<sup>19</sup> showed that animals subjected to chloroform were better able to withstand its toxic effect if a high carbohydrate diet was given previous to the administration of the drug and indicated that in those animals least effected, there was adequate glycogen stored within the liver, and in those most susceptible, there were marked fatty changes in the liver. The relationship between the amount of fat deposited in the liver and the susceptibility of liver cells to necrosis has been well shown, as have the merits of high carbohydrate intake in decreasing the fat within the liver cell.

Glucose has long been advocated in the preoperative preparation of jaundiced patients to prevent postoperative bleeding, but until Ravdin's report<sup>17</sup> in 1930 calcium was given in addition to the glucose and it was thought by many that the calcium was the responsible agent. Calcium has had quite a vogue in the preoperative preparation of the jaundiced patient. The basis for its introduction was a fallacious assumption that there was a deficiency in blood calcium in the jaundiced individual. Since calcium is necessary for clotting of blood, the concept that there was a deficiency of calcium in jaundice formed a rational basis for explaining the bleeding tendency and resulted in much clinical data regarding the value of calcium therapy. In the light of the knowledge of the effectiveness of glucose to protect the hepatic cell, it is unfortunate that it is difficult to determine whether, in addition to calcium, glucose was also given; therefore much of the older data in regard to calcium therapy is of no value. Suffice it to say that there is no lack of calcium in the blood of the jaundiced patient, nor is there, as Gunther and Greenberg<sup>20</sup> have so well shown, a lack of availability of the calcium present except in the presence of a low plasma protein. This latter contribution has clarified our concept concerning the bleeding tendency in jaundice decidedly since in association with the view that there was a decrease in blood calcium in jaundice, there have arisen many theories regarding the cause of the bleeding, based upon a combination of calcium with bile salts, bilirubin, or some other substance which prevented its activity. Calcium is still being advocated<sup>21</sup> in treatment of the jaundiced patient, but at least it has been stripped of the prestige of a scientific basis.

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Following occlusion of the common duct, the bilirubin level of the blood, as measured by the van den Bergh test, increases. This increase continues with an associated increase in generalized icterus for a variable period of time when, despite the fact that there is complete obstruction to outflow of bile from the liver, the serum bilirubin level reaches a plateau. When this plateau has been maintained for several days, we feel that the patient has become stabilized under the new environment and is best able to stand operation. We do not operate on patients with rising or falling levels of serum bilirubin. The mechanism for the stabilization of the level of serum bilirubin is not understood, but it is our experience that the patient withstands operation better and has less tendency to bleed after stabilization has occurred.

In the preparation of the patient for operation there are two objectives: (1) that the patient's general physcial condition be made as good as possible, and (2) that the hepatic parenchyma be restored to as nearly normal as conditions permit. The complication most feared is bleeding either before or after operation, and this complication is better prevented.

Following operation, similar conditions as obtained before operation are present and are treated in much the same manner. The release of obstruction to the outflow of bile does not immediately correct the effects of the obstruction. Bleeding which is not common before operation is to be feared because of the added source of hemorrhage, the fresh wound. Even when all visible bleeding points have been carefully tied at operation, there is a certain amount of oozing. The clot which forms is grossly abnormal in that it does not retract well. Much of the fresh postoperative bleeding is due to bleeding behind a clot, a mechanism which is well known to cause continued bleeding even in normal wounds. In many instances were it possible completely to clean out the old semi-formed clot and allow for drainage of the blood, bleeding could be more easily controlled. Packing over the clot is a maneuver of little value, as it is in wounds in individuals with normal clotting mechanisms.

The causes ascribed for the bleeding tendency associated with jaundice consist not only of deficiency of any one of the elements concerned with clotting, but the presence of substances which are known to prevent clotting. The question of the relationship of calcium to bleeding in jaundice has been discussed above. Fibrin insufficiency has been suggested chiefly on the basis that the liver is a rich source of this material. Melchior<sup>29</sup> noted a marked decrease in blood fibrinogen and thrombin after hepatectomy in dogs. Moss<sup>30</sup> and Ravdin, Riegel and Morrison<sup>16</sup> have shown that there is not a deficiency in fibrinogen in jaundice. Barlik<sup>31</sup> was impressed with the liver as a storehouse and regulator of the antiprothrombin content of the blood and concluded that with liver damage this mechanism is lost. Bile salt increases in the blood have been surmised to occur in obstructive jaundice, and their presence was

With regard to the value of glucose in jaundiced cases, the opposite is true. Not only has the value of high carbohydrate intake been indicated by clinical data, but experimental studies as well have stressed its merit.

Not only does the glucose afford protection for the liver, but it is of importance in reparative processes after liver damage, as has been recently reemphasized by Snell and Bollman.<sup>22</sup>

An additional safeguard against liver damage is the administration of whole blood. The effects of anoxic states on the reaction of the liver to damage have been demonstrated by Goldschmidt, Ravdin, and Lucké,<sup>9</sup> and Judd, Snell, and Hoerner.<sup>23</sup> The mechanism for the effectiveness of blood transfusions in liver damage is not well understood, nor is it demonstrable from studies on the blood in jaundiced patients that there is consistently a decrease in the oxygen-carrying capacity. The transfusion of blood in jaundiced patients is not to be reserved for patients who bleed postoperatively, but is valuable as a preventive measure. New blood with normal clotting mechanism introduced into the patient has a rational basis in the supply of the necessary elements for clotting, and it undoubtedly is an important factor in prevention of and restoration from hepatic damage.

One of the most difficult questions relative to the jaundiced patient concerns the determination of the time when the patient is properly prepared for operation. Clute and Swinton<sup>24</sup> suggest a preoperative regime for five to twelve days. Ewald<sup>2</sup> states that one should wait no longer than two to four weeks but that longer periods of waiting even up to a year may not be particularly damaging. It is quite difficult to see the value of any time limit for the preparation of the patient, as many variable factors other than time may be present to influence the amount and nature of damage to the liver. There has long been the hope that some means of measuring accurately the bleeding tendency would afford a reliable test for deciding the time of operation. This has not been the case. Likewise liver function tests theoretically offer this possibility, but actually none of the tests of liver function has proved of merit in the determination of the possibility of bleeding in the jaundiced patient. This is probably due to the fact that the present methods are not definitive enough since they test only one or another phase of liver activity. Even when several tests are used routinely, the results are disappointing.

In 1930 Linton<sup>25</sup> reported that the sedimentation rate of the blood was useful in determining whether or not patients would bleed postoperatively. However, subsequent experience<sup>26, 27</sup> has not shown this to be the case. The sedimentation rate may be affected by many factors associated with jaundice, and it is hardly to be expected that this test would be distinctly prognostic.

fluffy yellow crystals which can be preserved indefinitely. This material may be prepared from clean fresh human drainage bile or from fresh ox bile. We feel that lyophilized ox gall bladder bile is better than human drainage bile because of the presence of bile salts in high concentration.

The management of the T-tube drain presents several interesting and important considerations. Frequently during the first few days the material draining from the T-tube will appear bloody. It has been suggested that the cause for this is the sudden decompression of bile ducts.<sup>34, 35</sup> Slow decompression such as is commonly practiced in relation to the urinary tract in retention has been suggested. This is practically impossible to accomplish since the common duct must be opened for the introduction of the T-tube and the loss of even a few cubic

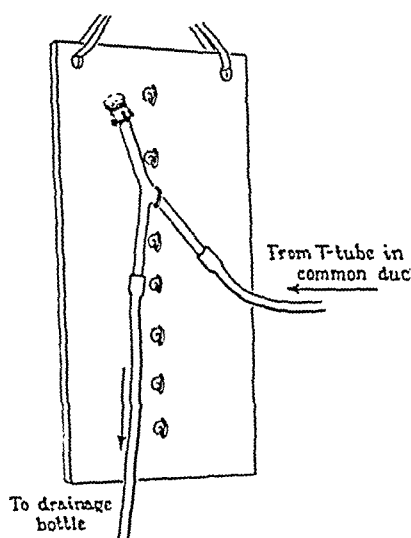


Fig. 1.—Simple method for gradual decompression of the common bile duct.

centimeters of bile from the ductal system will reduce the pressure markedly. What is probably more true is that following drainage of the common duct, the intraductal pressure is suddenly decreased from a value of about 300 mm. of water not only to zero, but even lower, because actual suction is applied by the habit of allowing the tube to drain into a bottle on the floor. By this means there is exerted by the drag of the column of bile a suction on the common duct of several feet of water. This can be overcome by several methods. The simplest is the use of a small bottle lying next to the patient at the level of the abdominal wall as suggested by Reid<sup>36</sup> or the use of a tube extending into the bottle, large enough to break the bile column. Methods more easily controlled which produce a reasonable intraductal pressure and allow the bile to be collected in a receptacle on the floor are prepared by placing an impediment to the outflow of bile. This can be accomplished by one of



assumed to interfere with clotting, either by direct action or by combining with elements necessary for clotting. Petren<sup>31, 32</sup> was able to increase coagulation time in vitro by the introduction of bile salts, but it was necessary to increase the bile salts to 0.2 per cent, a value much higher than has been found in the blood by many authors. Methods for analysis of bile salts in blood are not dependable, and a high bile salt level is not likely to be maintained. Bollman and Mann<sup>5</sup> found that bile salts are rapidly excreted if injected into the blood stream. Carr and Foote<sup>27</sup> present an unusual theory for the hemorrhagic tendency in jaundice. These authors assume that cysteine and mercaptans are increased in the blood in jaundice and that these substances are responsible for inhibiting clot formation.

The causes of the bleeding tendency have not been determined. All of the elements necessary for clotting have been suspected as being deficient, but collected data have not substantiated these assumptions. In addition, the presence of substances which might prevent clotting has not been proved. The knowledge of methods of preventing and treating bleeding in jaundiced patients has progressed farther than has the knowledge of the causes underlying the bleeding tendency in jaundice.

Postoperative bleeding in the jaundiced patient is best treated by attention to the wound, by frequent blood transfusions, and by the introduction of glucose solutions by vein. When bleeding continues despite these measures, it is worthwhile to remove the drainage tube from the common duct to prevent irritation from the tube.

Fluid intake should be controlled by supplying adequate fluids and salt to overcompensate for that lost not only through the usual channels, but also from the drainage of bile. For this reason, it is necessary to estimate total fluid loss. Continued loss of bile will cause the patient to lose not only large quantities of bile which are so necessary to digestion and assimilation of food, but also the constituents of bile, which loss constitutes a drain on mineral stores. This may be compensated for by returning the bile drainage to the intestine by use of the Jutte or Levine tube. This method of returning bile to the patient is usually troublesome, not only to the patient, but to the doctor as well. Even if carefully collected over twelve-hour periods, the bile has a tendency to spoil and is unpleasant to administer. To overcome this objection we have prepared lyophilized bile which can be given in tablet or capsule form. Lyophilized bile is quite different from ordinary tablets of *fels bovis* in that it will dissolve in water to form a substance resembling the original sample of bile from which it was prepared, not only in composition but in consistency, odor, and color. The material is prepared after the method of Flosdorf and Mudd<sup>33\*</sup> and forms from the bile light

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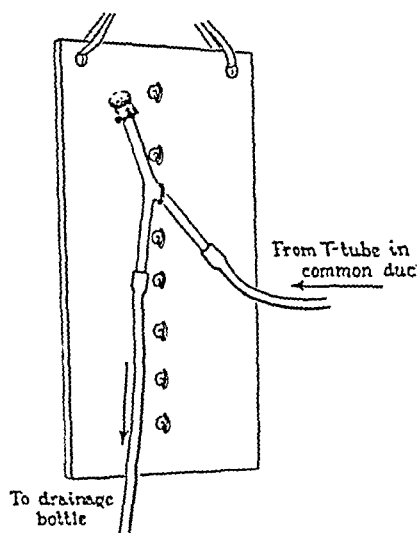


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patients. The problem of the jaundiced patient is not a simple problem concerned with the release of mechanical obstruction to the outflow of bile. The patient with obstructive jaundice is ill from the effect of changes incident to the obstruction and suffers from an illness which is widespread in its effect. The attack on the local problem must wait until the patient is properly prepared and attempts are to be made to simulate normal physiologic conditions as closely as is possible throughout the entire course of treatment.

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two simple methods. The first is one commonly used in decompressing the urinary bladder. One arm of a glass Y-tube is connected to the T-tube in the common duct; another arm is connected to the collecting receptacle. The third arm is covered with sterile gauze to prevent contamination, but otherwise is left open to provide a vent for breaking the column of bile. The glass Y is then attached to a board, the height of which may be adjusted to any desired pressure level (Fig. 1).

This apparatus is quite effective and easily prepared and controlled. A somewhat more elaborate apparatus for controlling intraductal pressure and which has a pressure-recording device attached may be made by the use of a glass pressure box through which courses a loose thin rubber tube. Air forced into the pressure box compresses the tubing and prevents the exit of bile until the pressure in the duct reaches a pressure higher than that exerted within the pressure box (Fig. 2).

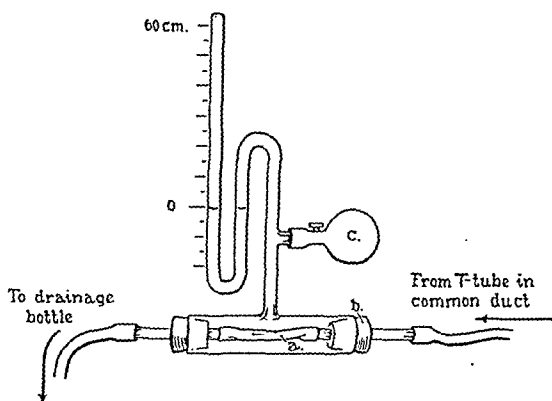


Fig. 2.—Author's method for decompression of the common bile duct.

Removal of the T-tube from the common duct should be accomplished as early as possible to prevent excessive loss of bile and ascending infection into the bile ducts. It is wise before the tube is removed to inject iodized oil under fluoroscopic control to determine whether the duct is patent to the duodenum. Even though the common duct is carefully explored at operation, it is possible for stones to be overlooked and visualization of the duct with a radiopaque substance is of value. If stones are present, they may be dissolved by the injection of ether as suggested by Pribram.<sup>36</sup> The tube should not be removed until it is ascertained that there is free passage of bile into the common duct.

In addition, to the prevention of suction on the common duct, these methods maintain a steady gentle pressure within the common duct, tend to force bile into the duodenum, and minimize the amount of bile lost through the drainage tube.

In the management of cases of obstructive jaundice, the care before and after operation is of importance not only in the prevention of post-operative deaths, but also in the early restoration to health to these

of unsuspected stones in the common bile duct always should be remembered in operating on the gall bladder. Most stones of the common duct can be palpated with the thumb and forefinger. However, some stones, when single and small and when in the ampulla, cannot be palpated. In these cases and in all other cases of stone of the common duct, however, the presence of the stones is indicated by enlargement of the duct or by change in its color. When the common duct is opened and explored and stones have been removed, exploring scoops of increasing size should be passed gently through the sphincter of Oddi into the duodenum. This will permit overlooked, small, hepatic stones to pass the sphincter into the duodenum. I think it is well to emphasize again that, if patients have or have not undergone previous operations on the biliary tract, the absence of jaundice does not exclude the possibility of stone in the common bile duct. In addition, stones in the common bile duct may manifest themselves clinically only by producing intermittent fever, and sometimes this fever is not associated with attacks of abdominal pain.

#### OBSTRUCTION OF THE BILIARY TRACT AS THE RESULT OF INFLAMMATORY LESIONS IN THE HEAD OF THE PANCREAS

In approximately 10 per cent of a group of 500 patients on whom I have operated for benign, obstructing lesions of the common bile duct, I have failed to find stones in the common bile duct when it was opened and the interior carefully explored. In these cases there has been an inflammation of the pancreas, cholangitis, and the bile frequently has been turbid. Culture of the bile has revealed, in most instances, a Gram-negative bacillus, either in association with, or not in association with, streptococci and staphylococci. In most of these cases the gall bladder is inflamed and infection can be demonstrated to have extended from the gall bladder, through the wall of the common bile duct and probably through the adjacent lymphatics to both pancreas and liver. In these cases removal of the gall bladder and prolonged drainage of the common bile duct have sufficed, in practically all cases, completely to eradicate the attacks of pain and jaundice. Many of these patients have been followed for a period of five years subsequent to operation.

There is a group of deeply jaundiced patients, in exploration of whose abdomens a tumor is found in the head of the pancreas. The tumor usually is thought to be malignant, and usually it is; but some of these patients, subsequent to cholecystenterostomy performed for relief of the biliary obstruction, have remained well for periods longer than five years. In a group of 113 patients<sup>22</sup> on whom cholecystenterostomy was performed at the Mayo Clinic for tumors of the head of the pancreas, 15 per cent were living and well five years after operation. This leads to the assumption that the lesion in the head

# PERSONAL EXPERIENCES IN THE TREATMENT OF BENIGN OBSTRUCTING LESIONS OF THE BILIARY TRACT

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AS a participant in the symposium on the liver and gall bladder I have been asked to discuss obstruction of the common bile duct exclusive of malignancy. In view of the desire of the editors of SURGERY that the papers shall cover only essential details, I shall discuss briefly the following: (1) the causes of obstruction of the common duct; (2) some of the factors which might lead to failure to recognize the condition when it is unassociated with jaundice; (3) the recent investigations by Butsch, McGowan, and me<sup>3, 4, 5</sup> of biliary pressure associated with biliary colic; and (4) the recent studies of McGowan and Knepper on duodenal motility and its effect on the common bile duct. The investigations and studies mentioned are of clinical significance to that group of patients who continue to have biliary colic subsequent to cholecystectomy and exploratory choledochostomy.

Benign obstructions of the common bile duct are the result of (1) calculi formed, for the most part, in the gall bladder and extruded through the cystic duct into the common duct; (2) inflammatory lesions of the pancreas and of the wall of the common bile duct and of the intrahepatic ducts; (3) inflammatory tumors of the head of the pancreas with and without duodenal ulceration; (4) strictures of the common bile duct, usually traumatic in origin; (5) benign tumors of the common bile duct such as neurofibromas; and (6) functional spasm or inflammation of the sphincter of Oddi or of the duodenal portion of the common bile duct.

## STONES OF THE COMMON BILE DUCT

The most common cause of obstruction of the common bile duct is biliary calculus. These stones, for the most part, are formed in the gall bladder and enter the common duct through the cystic duct. Such stones are usually faceted, although occasionally they may be ovoid. In some instances primary stones will form in the common bile duct. These are usually soft and are composed, for the most part, of bile pigment. Whereas it is usually thought that the presence of stone in the common bile duct manifests itself by typical attacks of biliary colic associated with jaundice, such is not always the case, for frequently stones in the common duct may produce biliary colic without jaundice or a feeling of discomfort subsequent to eating and without the nausea that results from pylorospasm. The possible presence

possible, however, to employ this procedure. In order to do so, it is necessary that sufficient duct be present above the stricture and that the duodenum be susceptible of sufficient mobilization to allow accurate anastomosis. When this is not the case and the stricture is found to involve practically the entire length of the duct, the surgeon has to be content either with establishment of an external biliary fistula, to be coned out and transplanted into the stomach or duodenum at a later time, or with insertion of a catheter or T-tube, one end of which is in the intrahepatic duct and the other in the duodenum, bridging the gap between with adjacent tissue, occasionally with omentum. Removal or passage of such tubes is almost always followed by recurrence of the stricture. Such an undesirable outcome is avoided when accurate choledochoduodenostomy or hepaticoduodenostomy has been made. In a few cases of small, localized stricture of the common bile duct, not completely obstructive, excision of the strictured portion, with anastomosis of the normal ends of the duct, has been followed by good results. When, however, scar tissue is allowed to remain, even though the lumen of the duct has been increased by application of the Heineke-Mikulicz principle, the scar tissue previously formed, associated with that which follows the plastic procedure, again may produce obstruction of the duct.

In a group of 29 cases in which resection of the common or hepatic bile duct or the ampulla of Vater was performed and which I reported before the meeting of the Southern Surgical Association in 1931,<sup>19</sup> recent follow-up studies have been made; 48.3 per cent of the patients were living and well more than five years after operation. To date, my series of strictures of the common bile duct numbers 51 cases with a hospital mortality for the entire group of 13.7 per cent.<sup>12, 13, 21</sup> Most of these patients were deeply jaundiced at the time of operation. The result in all operations for stricture, providing accurate anastomosis can be made between the stump of the duct and the duodenum, is dependent on the degree of infection of the wall of the duct itself as well as that of the liver, for, if an unusual amount of inflammation exists in either of these structures, the obstruction may recur.

#### BENIGN TUMORS OF THE COMMON BILE DUCT

Benign tumors of the common bile duct are exceedingly rare; most tumors involving the extrahepatic biliary ducts are malignant.

In 1930 I operated upon a patient who had a localized neurofibroma, 1 cm. in length and 1 cm. in width, at the junction of the common and hepatic ducts.<sup>5</sup> The neurofibroma was excised and the two ends of the hepatic duct were anastomosed with the end of the common bile duct. Although the patient had some evidence of a mild degree of obstruction of the common duct during the first year and in the



of the pancreas in this 15 per cent was not malignant but inflammatory. In such cases, although a section removed from the head of the pancreas would clarify the diagnosis, the risk of such a diagnostic procedure has not been thought to be warranted in the light of the fact that the surgical treatment employed is practically identical, whether the tumor is inflammatory or malignant. That this percentage of patients, who were afflicted as has been described, lived longer than five years after operation, not only makes the outlook for such patients more hopeful but affords an argument in favor of surgical procedures for them.

On several occasions I have operated on patients who had ulcers in the posterior wall of the duodenum, with perforation into the pancreas. Symptoms were identical with those of disease of the biliary tract. The intermittent pains and obstruction of the common duct in these cases were attributable to the perforation of the ulcer into the pancreas and the associated edema of the pancreas, which produced stasis in the pancreatic portion of the common bile duct. In these cases a previous history of a type of dyspepsia characteristic of ulcer assisted in the differential diagnosis, and gastroenterostomy usually has resulted in healing of the ulcer and relief of symptoms. It should be a routine, therefore, in the course of all operations on the biliary tract, particularly when there is a question of intermittent obstruction of the biliary tract, to palpate both the posterior and anterior walls of the duodenum. This examination should be made even though roentgenologic examination of the duodenum may have given a negative result, for occasionally ulcers are situated so low in the posterior wall of the duodenum that they may be overlooked in the roentgenologic examination.

#### STRICTURES OF THE COMMON BILE DUCT

Strictures of the common bile duct usually are traumatic in origin and manifest their presence by a history of prolonged biliary drainage subsequent to operation on the gall bladder or by the appearance of jaundice soon after such a procedure. In an occasional case obliterative cholangitis may be the cause of the stricture of the common duct.

The treatment of stricture of the common bile duct, and also of external biliary fistula associated with stricture of the common bile duct, always is surgical. Although various procedures have been described, the most effective and lasting in their beneficial results have been choledochoduodenostomy or hepaticoduodenostomy. This is an anastomosis between the stump of the duct above the stricture or above the fistula and an opening in the duodenum. An accurate anastomosis is made between the edges of the duct and an opening made in the duodenum, thus obtaining a mucous membrane union. It is not always

some cases morphine produced spasm of the second portion of the duodenum and that it produced, also, what appeared to be spasm of the sphincter of Oddi, with increase in the pressure within the common duct. When amyl nitrite or nitroglycerin was administered, the spasm of the duodenum subsided, the lower end of the common bile duct relaxed, the brominol left the intrahepatic and common ducts and entered the duodenum, and relief of pain was obtained.

In some cases in which biliary colic continued subsequent to operation on the gall bladder, these conditions of spasm were found to occur both in the presence of, and in the absence of, stones in the common duct. It should be emphasized that stones in the common duct are usually the cause of such recurring colic and always should be regarded as the probable cause of the pain until the duct has been opened and thoroughly explored for stones. When stone is not found, however, the possibility that the spasm of the sphincter of Oddi or of the duodenum is a causative factor must be borne in mind. If the former, dilatation of the sphincter of Oddi frequently will give relief of the pain; whereas, if the pain is attributable to increased duodenal pressure from spasm, reduction in intraduodenal pressure can be accomplished by duodenojejunostomy as Gray has demonstrated. This has been tried and, although too short a time has elapsed to be certain of the end results, relief of the increased duodenal pressure and relief of pain have been demonstrated.

#### JAUNDICE, A COMPLICATING FACTOR IN OBSTRUCTION OF THE BILIARY SYSTEM

Jaundice complicating obstructing lesions of the common bile duct introduces the tendency to excessive bleeding following surgical procedures. Jaundiced patients need scarcely ever be considered as candidates for immediate or emergency surgical procedures. This is particularly true when it appears that the jaundice has been fluctuating in intensity. A period of delay allows study of the function of the kidneys, the liver, and the other parenchymatous organs and makes it possible to know the progress of the jaundice and particularly whether it is subsiding. Operation should be delayed until maximal reduction in jaundice has occurred. Studies of the coagulation time of the blood in such cases afford valuable indices not only of the tendency to bleed but also of the function of the liver. In my experience, a prolonged coagulation time, when a patient has been jaundiced, usually has indicated more damage to the parenchyma of the liver than can be considered an average amount for jaundiced patients.

Whereas the method of studying coagulation of the blood described by Lee and White afforded valuable gross evidence of wide variations in coagulability of the blood, the introduction by Nygaard and Baldes<sup>1, 2</sup> of a physicoelectric method in which, by means of a photoelectric cell

years following, she was without evidence of disease of the biliary tract in 1935 when Comfort and I<sup>6</sup> reexamined her.

#### SPASM OF THE SPHINCTER OF ODDI AND OF THE DUODENUM

The introduction of choledochography, or visualization of the common and hepatic ducts after introduction of an opaque substance, such as brominol or lipiodol, has assisted materially in studying the pathologic physiology of the common bile duct. Not only do choledochograms afford an indication of the size of the duct but they also reveal the presence of persisting filling defects attributable to stone; of persisting obstruction the result of pancreatitis, both with and without reflux of the media up into the duct of Wirsung; of persisting inflammation of the lower end of the common bile duct; or of sphincteritis or spasm of the sphincter of Oddi. Although it is recognized that persisting stones in the common duct will cause persistence of symptoms of disease of the biliary tract, it is not generally recognized that pancreatitis may continue to do the same thing. Visualization of the common bile duct by choledochography has shown, however, that persisting pancreatitis will cause, in the common bile duct, continued stasis which may be responsible for recurrence of pain as well as possible recurring formation of stone in some cases.

The problem of abnormal function of the sphincter of Oddi has been called to attention by Mirizzi, by McGowan, Butsch and Walters, by Walters and Thiessen, and by Pavel.<sup>15, 16</sup> The last named author described cases of spasm of the sphincter of Oddi producing jaundice. Butsch and McGowan, of the Mayo Foundation, combining studies of choledochography with studies of pressure within the common bile duct, found that the pressure within the common ducts of patients who had biliary colic attributable to spasm of the sphincter of Oddi, increased to as much as 200 or 300 mm. of water.<sup>3</sup> Using a substance opaque to the Roentgen rays to measure the intraductal pressure in these cases and examining the duct under the fluoroscope, they demonstrated that in the presence of spasm of the sphincter of Oddi many of the smaller intrahepatic ducts filled. With the administration of amyl nitrite or nitroglycerin, spasm of the sphincter of Oddi subsided, pain ceased, intraductal pressure dropped to within normal limits, and the opaque substance left the hepatic and common ducts. To determine whether this effect was confined to the sphincter of Oddi alone, or whether it might involve the duodenal portion of the common bile duct, studies of intraduodenal pressure were carried out by McGowan and Knepper, of the Mayo Foundation. These investigators injected barium into the duodenum through a duodenal tube orally inserted and injected brominol into the common bile duct. On examining these structures by fluoroscopy, the investigators were able to show that in

those of biliary colic occurred. A few cubic centimeters of ether were introduced into the common duct through the T-tube, as suggested by Pribram, at first undiluted and then mixed with an ethyl alcohol oily substance. This produced visual fragmentation of the shadow of what had seemed to be a single stone. Consequently amyl nitrite was administered in the course of an attack of pain and apparently relaxation of the lower end of the common duct occurred, allowing the fragmented particles of stone to be expelled spontaneously into the duodenum. Subsequent cholelithograms gave evidence of a normal looking common bile duct. Closure of the T-tube for more than ten days was not followed by any discomfort and since the T-tube has been removed the patient has not had abdominal discomfort. On other occasions, even as long as three months subsequent to cholelithostomy, persisting pancreatic obstruction has been noted and has subsided after more prolonged drainage.

### SUMMARY

The condition which most frequently produces obstruction of the common duct is biliary calculus. Less frequent causes of obstruction are inflammatory lesions of the pancreas, associated with cholangitis and strictures of the common bile duct. Jaundice, as well as chills and fever, may be absent. Stones in the common bile duct manifest their presence by enlargement of the duct or changes in its color and, if the common bile duct is enlarged, it should be opened and searched for stones with exploring scoops. In an occasional case of stone in the common duct the only symptom will be pylorospasm or intermittent fever.

Inflammatory tumors of the head of the pancreas may simulate carcinomatous tumors. Such enlargements may occur primarily, or secondary to infection in the gall bladder, or secondary to perforating ulcers of the posterior wall of the duodenum.

Strictures of the common bile duct are usually traumatic in origin and are best treated by cholelithoduodenostomy or hepaticoduodenostomy if sufficient duct remains above the stricture to allow its anastomosis with the duodenum by means of an opening in the latter structure.

Recent studies by McGowan, Butsch, and Knepper on the effect of spasm of the duodenal portion of the common bile duct or of the sphincter of Oddi have shown that such spasm, occurring in human beings, can cause a type of pain similar to that of biliary colic, with increased pressure in the common bile duct and in the duodenum. With administration of amyl nitrite or nitroglycerin the spasm disappears, accompanied by relief of pain and a drop in pressure within the duodenum and within the common duct. These manifestations may be the accompaniment of stone in the common bile duct and the fact that a stone is not present can be determined only by intraductal exploration.

and an electric recording apparatus, an exact curve of the rate of blood coagulation can be recorded has been of great value. By giving an indication of disturbed coagulability prior to, as well as subsequent to, operation, this apparatus has given the first indication of approaching hemorrhage.

By far the greatest aids to hastening the coagulability of the blood of jaundiced patients have been solutions of glucose and of calcium chloride given intravenously and blood transfusion. Glucose and calcium chloride, intravenously injected, have been used as a routine, in preparation of jaundiced patients, at the Mayo Clinic since 1921.<sup>18</sup> These injections have been supplemented by blood transfusion given the day prior to operation if the patient has been deeply jaundiced or if the jaundice has been present for more than an average time. When the jaundiced patient is operated upon, surgical treatment should be directed toward relief of biliary obstruction with as little disturbance of tissue as possible. To this end I have frequently resorted to cholecystostomy rather than to cholecystectomy, since removal of the obstructing lesion in the common bile duct is the point to which surgical attention of necessity is directed. At the same time, of course, stones in the gall bladder should be completely removed to prevent their entering the common bile duct at a later time, causing the biliary obstruction to recur. From my having operated upon approximately 500 such patients in the last twelve years, I have become convinced that for deeply jaundiced patients the decreased risk of cholecystostomy, as a part of the removal of a stone from the common duct, far overshadows the fact that in a few of these cases it will be necessary to perform cholecystectomy at a later time.

#### CHOLEDOCHOGRAPHY

Following the recommendations of Overholt, Mirizzi, Bartlett, and others, choledochography has been a postoperative routine on my service at the Mayo Clinic since 1934. I do not remove a T-tube inserted in the common bile duct at the time of operation until postoperative choledochograms have revealed that the previously dilated duct has returned, subsequent to operation, to normal size and that there are no visual filling defects apparently attributable to stones retained in the duct. The advantages of such methods of study of the common bile duct have been stressed in previous communications.<sup>20, 23</sup>

#### CASE REPORT

In a recent case the patient was an obese man, 50 years of age, on whom cholecystectomy had been performed elsewhere and from whose common bile duct one stone had been removed at the clinic. Postoperative choledochograms revealed a circumscribed, negative shadow in the lower portion of the common bile duct, as though a stone were present. When the T-tube was closed, symptoms resembling

## LIGATION AND REFRIGERATION OF INTESTINE

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IT HAS been shown elsewhere<sup>1</sup> that the limbs of animals can withstand at least 15 hours of deprivation of blood at room temperature and periods of up to 54 hours at ice temperature. On the other hand, slight elevations of temperature greatly shorten the period of endurance. The literature dealing with both the tolerance of local asphyxia and the constitutional effects (shock) has been considered in other papers.<sup>2</sup>

Valid comparisons between the resistance of the peripheral tissues and of the viscera, therefore, can only be made at identical temperatures. This point, which is purely theoretical, was not tested experimentally. It was established, however, that the abdominal viscera differ rather widely among themselves in resistance to asphyxia, and from the data it appears possible that some of them, at least, are as resistant as the limb tissues at the same temperature.

Although the intestine is one of the more resistant of the abdominal viscera, surgeons seem to agree that it cannot survive more than six hours of complete lack of blood. In considerably less time than this it suffers damage which is expressed in dark discoloration, atony, and subsequent severe inflammation. An exact time limit under practical clinical conditions will probably be hard to establish, because infection, intoxication, and particularly fever must greatly reduce the period of resistance as compared with the normal bowel. This survival period is not exceeded in any warm-blooded species of animals and in some of them the limit is much shorter, perhaps because of higher body temperature or more active metabolism. Thus, the rat intestine seems to slough after 2 to 3 hours without circulation and that of the rabbit, after about 4 hours.

On the other hand, physiologists commonly keep various organs or tissues at refrigerator temperatures for periods of days, with retention of even the finer functions. As early as 1913, Cannon and Burket<sup>3</sup> pointed out that, when a piece of small intestine is kept on ice for 24 hours and then placed in warm saline solution, the occurrence of rhythmic contractions demonstrates preservation of the myenteric plexus. Their description of similar preservation for 6 or 7 hours when the vessels were merely ligated leaves it uncertain whether the bowel was exposed to body or room temperature.

As far as known, the present experiments are the first dealing with refrigeration of intestine in situ and subsequent restoration of circula-

The presence of jaundice in a case of biliary obstruction requires particular attention to control the tendency to bleeding. Solutions of glucose and calcium chloride, given intravenously, and transfusion of blood form the most effective medical methods of combating this tendency. These methods should be applied preliminary to, and following, surgical relief of the biliary obstruction.

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tion. The results conform to the physiologic experience with isolated organs and with my observations on refrigeration of limbs. The reduced temperature necessarily favors tissue preservation by inhibiting local metabolism (oxygen consumption and accumulation of waste products). For the same reason, instead of causing shock, it practically abolishes shock effects.

Tests of this kind can be performed by selecting a loop of intestine, protecting each limb of the loop at its base together with the adjacent mesentery with thin gauze or muslin, and applying a rubber ligature around the cloth, tightly enough to stop circulation but with avoidance of extra tension which would unnecessarily injure tissue or vessels. The loop is then dropped back into the peritoneum and the laparotomy wound closed with temporary sutures until the end of the test period. For tests with refrigeration, the loop is kept outside the abdomen by sewing the edge of the cloth to the margins of the wound, and the abdominal wall is closed around it so as to expose the loop up to a trifle above the ligature. The animal is then secured in a holder having a suitable slot in the bottom, so that the loop can be submerged in iced saline solution up to the abdominal wall, without wetting more than a very small surrounding area. The jar containing the saline solution is set in another vessel containing a mixture of ice and salt, and a thermometer is used to stir the saline solution frequently so as to make sure that the temperature in the immediate vicinity of the loop is maintained as nearly as possible between 0 and 2° C. Apprehension was felt at first that the pressure of the ligature might cause necrosis of the bowel or thrombosis of its vessels, but, although this danger is real, it is minimized when the refrigeration includes not only the asphyxiated loop but also a narrow zone above the ligature.

A considerable series of experiments were first performed upon rats, with ligation of various lengths of intestine for various periods of 2 to 6 hours. It was easily established that the intestine after such treatment with refrigeration retains excellent color and tone without signs of gangrene. The mortality, however, was very high, evidently from chilling and exhaustion, in spite of attempts at artificial warming of the body, because the blood counts gave no indication of shock but the body temperatures fell very low. Larger animals, therefore, were used for continuing the experiments. The records shown in the table are illustrative.

Dr. A. S. Price kindly provided the following additional data for the blood of Cat D on the day of death; differential: large and small lymphocytes, 22 per cent; mature polymorphs, 60 per cent; immature polymorphs, 18 per cent; blood sugar, 98; urea, N 56, NPN 85; plasma, NaCl 480 mg. per cent.

At autopsy the heart and great veins of this cat were full of blood. Lungs were normal. Liver was moderately congested. Other viscera, including spleen and bone marrow, were grossly normal. Stomach was tightly contracted and empty except for a little pale yellow fluid; there were also signs of vomiting of such fluid. The perito-



TABLE I  
LIGATION AND REFRIGERATION OF INTESTINE

ANIMAL	PART LIGATED	DURATION HOURS	TEMPERATURE IN SALINE, C.	RECTAL TEMPERATURE, C.	LOCAL RESULT	SYSTEMIC RESULT
Rabbit A	10 cm. of empty small in- testine	7	2°	33-31°	Pink color, firm tone of loop	Uneventful recovery; no important changes in blood count
Rabbit B	10 cm. of cecum and colon full of feces	7	6°	33-31°	No discolor- ation or atony	Death in 8½ hours, with fever 39° C., red cells slightly in- creased, leucocytes reduced
Cat A	12 cm. of empty small in- testine	8	0-2°	32-31°	Pink color, firm tone of loop; no obsti- pation, diarrhea or disten- tion	Cat unwell; subnor- mal temperature; red cell count fell from 9.1 to 5.7 mil- lions in 15 hours; leucocytes rose briefly to 24,200; normal after 3 days
Cat B	10 cm. of empty small in- testine	16	2-5°	31°	Same	Weakness, anorexia; no vomiting or fever; blood changes similar to above; normal after 5 days
Cat C	Lower half of small in- testine, not all empty	4	2-8°	31-32°	Same	Temporary leuco- cytosis; gradual fall of red cells from 9.9 to 6.2 mil- lions in 2 days; anorexia, constipa- tion, marked pros- tration; recovery in 5 days
Cat D	Entire available intestine	3	2°	33°	Same	Brief leucocytosis above 100,000 cells; progressive fall of counts to 11,700 leucocytes, 2,700,000 red cells on sixth day; subnormal temperature, ano- rexia, trivial diar- rhea; increasing prostration to death on seventh day

brief time at room or body temperature, the reduction of adhesions by cold seemed definite and positive. In particular, the paralysis of the omentum by cold, so that it does not migrate or cling in the usual manner, is visibly evident during and after refrigeration. It seems probable that cold completely prevents the immediate formation of adhesions and thus allows slightly injured organs to repair themselves without forming attachments, but it does not prevent the later formation of adhesions when surfaces are too badly injured or stripped of peritoneal covering.

Several experiments were performed, without ligation, chiefly in rats by packing the peritoneal cavity with ice or irrigating it with iced saline solution while the animal was suspended in a warm bath to keep up the general body temperature. Also, animals which had developed peritonitis from accidental causes were treated similarly, with or without the use of antiseptics in the peritoneum, with the idea that the cold might retard the absorption of either toxins or chemicals. Cleansing of the peritoneum, which is considered practically impossible, might thus become feasible and the subsequent hyperemia conceivably might increase resistance. Though this work was not thorough or conclusive, it gave the impression that the method is useless because the infection is in the peritoneal tissue and not merely on its surface and also that the manipulations are harmful.

The same conclusion was reached in an experiment with a pure culture of *Staphylococcus albus*, selected as an organism of low virulence. The growth from one agar slant was emulsified in 30 c.c. of saline solution and divided in two lots of 15 c.c. each. These were injected intraperitoneally in two cats. Both vomited and were somewhat unwell within one-half hour. Laparotomy then was performed under amytal and a little ether. The spleen and entire intestine of one cat were brought out into a bowl of saline solution at about 38° C. and washed gently for ten minutes. The spleen and intestine of the other cat were similarly everted, their circulation cut off by long elastic clamps, and they were first painted with mercurochrome and then washed for ten minutes in successive bowls of iced saline solution. Both wounds were closed immediately after the treatment. The first cat recovered with scarcely any symptoms. The second died after three days with the abdomen full of white staphylococcal pus.

Though the resistance was evidently lowered by this treatment, it must be noticed that the entire peritoneum was infected, including parietal and other surfaces not included in the ligation and refrigeration, and these parts might have been affected injuriously. It was intended to perform other experiments more strictly localized, in which the everted bowel would be suspended in an iced bacterial suspension during ligation, but under the circumstances these could not be carried to any positive conclusion.

neum was free from exudate, its surfaces glistening, not inflamed. The intestine was empty throughout except for a trifle of fluid like that in the stomach and completely free from adhesions; the walls were firm and moderately contracted, completely free from signs of necrosis, inflammation, or edema. The gall bladder contained about 1 c.c. of turbid light yellow bile. A small amount of urine was free from sugar, acetone, and albumin. The brain and spinal cord were negative to inspection.

Microscopic report from Dr. Price: Lungs, pancreas, adrenals, thyroid, and parathyroids were essentially normal. There was simple passive congestion of liver, without fatty changes; slight lymphocytic infiltration in some portal canals; small amount of yellow pigment suggesting hemosiderin, chiefly within some of the hepatic cells, also in some Kupffer cells. Other sections of liver showed some simple toxic degenerative changes with beginning necrosis. Kidneys: no evidence of true nephritis. Glomeruli were moderately congested but well preserved. There was marked cloudy swelling and some degeneration in tubules; either hydropic or fatty vacuolation of cells in convoluted tubules; several focal areas of lymphocytic and monocytic infiltration in cortex. Spleen appeared somewhat collapsed, with prominence of muscle trabeculae and obliteration of follicles, with fibrosis where some follicles should be. Stomach was normal. Duodenum showed some cloudy swelling of the muscle fibers. "Sections from the intestinal wall show some loss in goblet cell formation, slight increase in acidophilic staining of the cells, and simple degenerative changes in the epithelium. There is no evidence of any marked degree of exudative peritonitis, although some sections do show the submucosa presenting an increase in lymphocytic infiltration in the perivascular areas." Smears of the marrow from femur and ribs appeared normal. The abdominal lymph glands showed some edema and congestion, with small areas of necrosis surrounded by reticuloendothelial hyperplasia. No blood cultures were taken.

Several other attempts of this kind gave the same type of result with still earlier deaths. Likewise, several trials with ligation of special portions of the intestine (upper part for endocrine possibilities, lower part for fecal absorption, etc.) proved fatal, partly or wholly because of the poor facilities.

#### OBSERVATIONS ON PERITONITIS

Two results of the work with intestinal ligations require additional mention:

1. The experiments were all performed with shaving or plucking of only a small area of the abdomen and with no attempt at asepsis; nevertheless, with all the ligations, of all durations up to 16 hours, symptoms or signs of peritoneal infection were never encountered. Although the rat and rabbit have very high natural resistance, the cat is reputed to be fairly susceptible to peritonitis. In the absence of controlled proof there is a possibility that the refrigeration and ligation may increase the local resistance, perhaps through the ensuing hyperemia. It at least seems certain that this treatment does not seriously lower the peritoneal resistance.

2. Adhesions were strikingly absent after all the ligations, except a few in places where the peritoneal surfaces had been considerably traumatized by the ligature. By comparison with a few animals in which the intestine had been similarly handled or ligated for a very

# EXPERIMENTAL ATTEMPTS TO PREVENT OR ABOLISH THE HYPERTENSION THAT IS ASSOCIATED WITH RENAL ISCHEMIA

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**A**N INGENIOUS method for the production of persistent hypertension in dogs has been described by Goldblatt and his associates.<sup>1</sup> It consists of constricting the main renal arteries by means of special silver clamps devised for the purpose. Many different experiments by various workers have been and are being performed in an effort to explain the mechanism of this type of hypertension. Much of the work has been reviewed recently by Goldblatt<sup>2</sup> and by us.<sup>3</sup> The prevailing evidence at present indicates that this type of experimental hypertension is due primarily to a humoral and not to a nervous mechanism initiated by ischemia of the kidneys. The nature of the hypothetical substance responsible for inducing the hypertension has not yet been determined.

The present paper deals with experiments in which an attempt has been made to gain additional information concerning the mechanism whereby renal ischemia induces the development of hypertension.

## METHODS AND RESULTS

Seven different types of experiments were performed. The method which was used for the blood pressure determinations consisted of puncturing the femoral artery with a needle that was connected to a mercury manometer.

*I. The Effects on the Blood Pressure of Connecting the Renal Vein to the Portal System Prior to Constriction of the Renal Artery.*—One of the prevailing theories in regard to the etiology of experimental renal hypertension is that the ischemia is associated with the formation of a pressor substance which, when liberated into the blood stream, causes a rise in the blood pressure. These experiments were performed in order to test the possible rôle of the liver in removing this hypothetical substance from the blood. Through an incision in the left flank, the splenic and renal pedicles were exposed. The left renal artery was occluded temporarily by a bull-dog clamp. The splenic and renal veins were divided and the distal end of the renal vein was anastomosed to the proximal end of the splenic vein, thus forcing a large part of the blood from the kidney to return to the heart by way of the liver. The clamp was removed from the artery and the incision was closed. These procedures alone at times resulted in a temporary rise in the blood pressure. Several

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The salient point established is that ligation combined with refrigeration seems to have a powerful effect in preventing shock, toxic absorption, and formation of adhesions, as well as maintaining the vitality of the tissues. It, therefore, might offer a promise of clinical usefulness in cases of extensive wounds or infections involving the intestine, if the single serious objection could be obviated. This obstacle is the fatal cachexia and anemia which have followed refrigeration of the entire intestine. Further experiments must decide whether this condition is due only to the crude methods necessitated by the lack of facilities, whether it is peculiar to cats or whether it represents a special disturbance of metabolic or other unknown character.

### CONCLUSIONS

1. Animals have survived the ligation and refrigeration of short loops of intestine for as long as 16 hours and of half of the small intestine for 4 hours.

2. Among the noticeable results at the end of such treatment are the rosy pink color and very firm tone of the intestine. Microscopically the walls show edema and some infiltration for a time, but there are no clinical symptoms of either obstruction or paralysis at any stage.

3. The formation of adhesions seems to be largely inhibited, though denuded areas necessarily form attachments later.

4. Resistance to peritoneal infection seems not to be lowered and may possibly be increased.

5. Some degree of cachexia and anemia follows every severe procedure of this kind. These have proved fatal in all experiments with ligation of the entire intestine. If further investigation proves this to be a specific disorder, it may possibly prove of interest to students of anemia.

6. If this difficulty can be removed, the method described may possibly become useful in certain surgical cases.

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days later, the right kidney was removed. After allowing the animal to recover from this operation, the left renal artery was partially occluded by a Goldblatt clamp.

Eleven experiments of this type were attempted but all except four were failures for various reasons. A rise in the arterial blood pressure occurred following the production of renal ischemia in the four experiments. The elevation in pressure was of approximately the same degree as one would have anticipated had the renal blood been emptying normally into the inferior vena cava instead of into the portal system.

II. *Effects of Renal Ischemia on Blood Pressure After Having Damaged Kidneys by Temporarily Blocking Renal Veins.*—It seemed possible, although unlikely, that severe damage to the kidneys might alter the response to a diminution in their arterial supply. For this reason, the renal veins of four dogs were completely occluded for an average period of four hours. A number of days separated the occlusion of the veins of the two kidneys. One of the animals developed a temporary rise in arterial pressure following these procedures alone. Following the recovery of the animals, the renal arteries were partially occluded by Goldblatt clamps, and all of them showed a definite rise in the arterial blood pressure. Except for some diminution in their sizes, the kidneys appeared essentially normal at autopsy.

III. *Effects of Constriction of Renal Veins After a Rise in Blood Pressure Had Been Produced by Partial Occlusion of Renal Arteries.*—It has been shown<sup>4</sup> that constriction of the renal arteries to the degree that results in hypertension is associated with a diminution in the renal blood flow and with a decline in the pressure in the renal arteries. It was thought that the rise in pressure in the kidney vessels which would be associated with constriction of the renal veins might result in a decline in the general arterial blood pressure. In two animals in which hypertension had followed partial occlusion of the renal arteries, the renal veins were constricted with Goldblatt clamps. The arterial blood pressure rose slightly in one experiment and declined slightly in the other, but the changes were no greater than those frequently encountered in this type of hypertension.

IV. *Effects of Constriction of Artery to Remaining Kidney When Adrenal Gland on That Side and Kidney on Opposite Side Have Been Removed.*—It has been shown<sup>2, 3</sup> that bilateral adrenalectomy prevents or abolishes hypertension due to renal ischemia. Cow<sup>5</sup> described a direct vascular connection between the medullary portion of the adrenals and the kidneys. He stated: "Under certain conditions adrenalin in appreciable amount is poured directly into the kidneys from the suprarenal bodies, producing a diminution in the flow of urine." It was concluded by Cow that the adrenals may be regarded as direct regulators of urinary activity. Since constriction of the renal artery results in a reduction in the pressure distal to the clamp and since the arteries to the adrenals are concerned in the collateral arterial circula-

tion that develops, it seemed possible, although unlikely, that the removal of the adrenal on the side of the remaining kidney might influence the response to renal ischemia.

Four experiments were performed in which the right kidney was removed, the left adrenal gland was removed, and, either immediately or several days later, a Goldblatt clamp was placed on the left renal artery. A definite rise in blood pressure occurred in all instances.

V. *Effects of Freeing Adrenals Except for Small Attachments Along Renal Pedicle on the Hypertension Associated with Renal Ischemia.*—As stated, it has been shown that bilateral adrenalectomy prevents or abolishes hypertension due to renal ischemia. Goldblatt<sup>2</sup> found that an amount of cortex without medulla close to the minimum requisite for survival still permitted the development of hypertension due to renal ischemia. The present experiments were performed in order to determine if a marked reduction in the blood supply to the adrenals would abolish the hypertension associated with renal ischemia.

Six experiments were performed on dogs with hypertension in which the adrenal glands were freed except for their attachments along the renal pedicle. Little if any alteration in the blood pressure followed this operation. Subsequently in several instances the adrenals were completely freed of all attachments and the blood pressure declined markedly.

VI. *Effects of Renal Ischemia on Blood Pressure When One Adrenal Has Been Removed and the Other Adrenal Has Been Completely Denervated by Transplanting It to the Neck.*—It has been noted previously<sup>3, 6</sup> that constriction of the artery to a kidney which has been denervated by transplantation results in an elevation in the blood pressure. As stated, renal ischemia is not associated with hypertension if both adrenal glands are removed. The present experiments were performed for the purpose of determining whether or not renal ischemia will result in hypertension if the adrenal glands are denervated. The most obvious manner of accomplishing this appeared to be to transplant one adrenal to another part of the body, such as the neck, and subsequently to remove the other adrenal. This method will be described subsequently but suffice it to state here that the adrenal was transplanted together with the adjacent kidney and this kidney was removed later leaving the adrenal in the neck. Following the removal of the nontransplanted adrenal, a Goldblatt clamp was applied to the artery of the remaining kidney.

Three experiments of this type were performed. In each instance a definite elevation in blood pressure was noted following the partial constriction of the artery to the remaining kidney. The results of an individual experiment follow and the blood pressure readings are given graphically in Fig. 1.

Protocol.—Large, male dog. Control blood pressures on Nov. 8, 9, and 10, 1937, were approximately 130 mm. Hg. Nov. 11, ether anesthesia, left kidney and adrenal



days later, the right kidney was removed. After allowing the animal to recover from this operation, the left renal artery was partially occluded by a Goldblatt clamp.

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One of the findings in distemper is an elevation in the temperature, and it was thought that the fever might be responsible for the decline in blood pressure that had been observed in some of the animals. For this reason, the effects of hyperpyrexia were studied. The two methods chosen for producing artificial fever were (1) exposure to an atmosphere with an elevated temperature and (2) the injection intravenously of 0.5 to 1.5 c.c. "double strength" typhoid vaccine. Three animals with hypertension were placed each day for from five to ten days in the warm compartment. The daily exposure was for approximately four hours. The temperature of the animal at the end of this time varied from 104 to 107° F. and there was usually a temporary decline in the blood pressure of from 10 to 20 mm. Hg. However, this decline was only temporary and it returned by the following morning to its previous level. A sustained reduction in the blood pressure was not encountered in the three experiments. The same was true in the one experiment in which hyperpyrexia was caused by injecting typhoid vaccine.

#### SUMMARY

The results of experiments which were performed in an attempt to prevent or abolish the hypertension that is associated with renal ischemia are reported. Partial constriction of the renal artery or arteries was common to all experiments. Efforts to influence the response to renal ischemia included (1) anastomosis of the renal vein to the portal system, (2) previous damage to kidneys produced by temporary occlusion of renal veins, (3) partial constriction of renal veins in presence of hypertension, (4) removal of adrenal gland on side in which renal ischemia is produced, (5) the freeing of the adrenal glands except for small attachments along the renal pedicle, (6) removal of one adrenal and denervation of remaining one by transplanting it to the neck, and (7) hyperpyrexia. All of these attempts were unsuccessful in altering the response of the blood pressure to renal ischemia. A severe illness such as distemper is usually accompanied by a decline in the elevated blood pressure that is associated with experimental renal ischemia.

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transplanted to neck. Organs without blood supply for thirty-five minutes. Blood pressure remained at essentially preoperative level. Dec. 13, right adrenal gland removed. Animal's condition remained about the same; blood pressure not altered. Dec. 20, transplanted kidney removed under local anesthesia, leaving left adrenal in neck. Condition of animal continued to be good, blood pressure unaltered. Jan. 19, 1938, right renal artery constricted by Goldblatt clamp,  $1\frac{1}{2}$  of  $3\frac{1}{2}$  turns. Jan. 21, blood pressure 148; Jan. 24, blood pressure 172; Jan. 26, blood pressure 185; Jan. 29, blood pressure 184; Jan. 30, blood pressure 200; Feb. 2, blood pressure 220; Feb. 3, blood pressure 236; Feb. 4, blood pressure 215 mm. Hg, dog vomited; Feb. 5, blood pressure 225; Feb. 7, blood pressure 230, dog quite sick, vomiting, convulsions, definite uremia, killed. Renal artery blocked at site of clamp by organized thrombus. Kidney appeared fairly normal. The transplanted adrenal was essentially normal both on gross and microscopic examination.

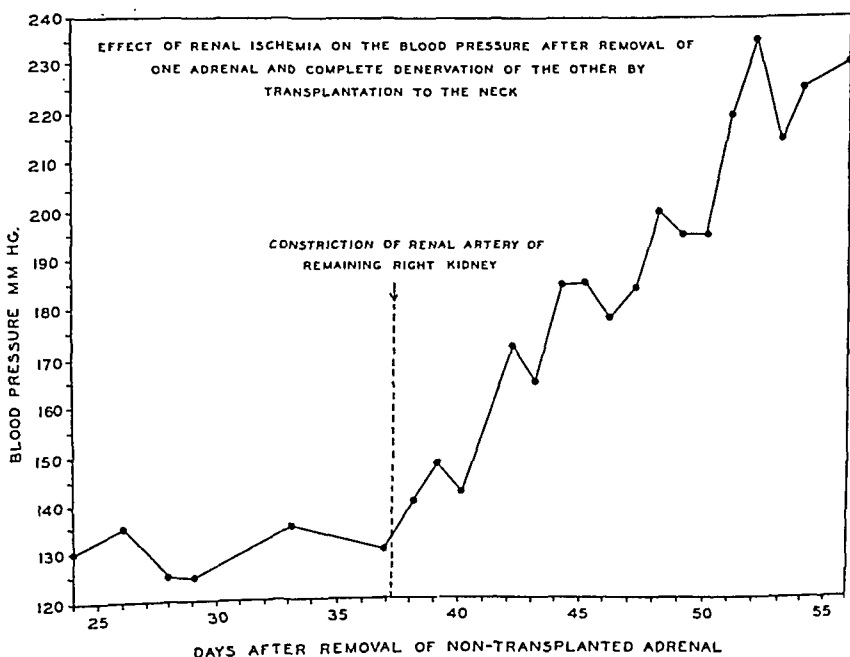


Fig. 1.—Showing the effects of renal ischemia on the blood pressure when one adrenal and one kidney have been removed and when the remaining adrenal has been transplanted to the neck.

VII. *Attempts to Abolish Renal Hypertension by Fever Therapy.*—We have the definite impression that it is more difficult to produce hypertension in dogs which are not in the best of physical condition than it is in entirely normal ones. Animals with nasal discharge and other evidences of distemper rarely respond with much elevation in blood pressure following constriction of the renal arteries. On a number of occasions, it has been noted that the elevated blood pressure of a dog declines if the animal develops distemper. Further, the decline was replaced subsequently by a rise in pressure in some instances when the animal recovered from the distemper. If a dog with hypertension developed severe mange or a virulent infection of any type, there was usually a decline in the blood pressure.

epithelium can be considered noncarcinomatous or at the most only pre-carcinomatous because it is within the confine of the so-called basement membrane." He recognized this change as occurring in both squamous and glandular epithelium and called it "carcinoma in situ."

Bouffannais (1929) reported the occurrence of a typical seminoma in an old dog. He observed that the tumor was of multicentric origin ("la genese pluricentrique"). Peyron (1936) noted that seminomas in dogs often confined themselves to the tubules. Peyron, Blanchard, Drieux, and Salomon (1936) remarked on the similarity between seminomas in human beings and dogs. They divided seminomas into two types—the seminal and the Sertoli cell type. The Sertoli cell type differed from the usual seminoma by forming good glandular structure. Deitermann (1937) studied twenty-seven cases of seminoma of the human testis, and was unable to demonstrate teratomatous tissue in any of them. Ectopic testes in the human have been regarded as particularly prone to the development of tumors.<sup>10</sup> This dictum would appear to be true for dogs also. Grenlich and Burford (1936) reported three seminomas of the cryptorchid testes of dogs.

#### MATERIAL

This study is based on 25 cases of spontaneous seminoma. These tumors were an incidental finding at post-mortem examination of dogs except in 1 case in which the tumor had metastasized and was the contributory cause of death. The involved testes were fixed in formalin; paraffin sections were cut on the entire testis and stained with hematoxylin and eosin.

These 25 seminomas were found in 22 dogs, in 3 of the animals the tumors being bilateral. Four seminomas were present in cryptorchid testes, in 1 dog a seminoma being present in each testis. On gross examination, testes containing seminomas were usually found to be enlarged, although a small proportion was found on routine sectioning in testes that grossly appeared perfectly normal. In those specimens in which the tumor was infiltrating, it appeared as a grayish mass of firm consistency.

#### HISTOLOGIC FINDINGS

Histologically, the seminomas were found to consist of cells that had large nuclei and prominent nucleoli, which stained deeply with basic stains. There was little cytoplasm around the nuclei. Mitotic figures were numerous. The most striking feature was the uniformity of the cellular picture, the cells varying little in size and shape (Fig. 1).

In 18 of the 25 seminomas it was apparent that the tumor had arisen from many foci in the seminiferous tubules rather than from a single focus (Figs. 2, 4, 6, and 7). In this group, the tumor was either wholly or partially in situ (Fig. 3). In 14 of these tumors the malignant cells

# THE PATHOGENESIS OF SEMINOMA OF THE TESTIS

## A HISTOLOGIC STUDY IN DOGS

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Experimental Medicine, the Mayo Foundation)*

THERE has been considerable difference of opinion in the past as to the origin of the testicular tumor which is variously called "seminoma," "embryonal carcinoma," "spermatocytoma," and "round cell sarcoma." Spontaneous seminomas in dogs are suitable for such a study as this, not only because their histologic appearance is identical with that of such tumors in man, but because, in dogs, seminomas are often found in an early stage of development. Among tumors of the human testes, it is unusual to find a seminoma which is not diffuse.

Langhans, in 1887, suggested that carcinoma of the testis arises from tubules in the region of the rete. He described the transition in certain early cases from glandular formation to solid tumor. Chevassu, in 1906, studied 128 tumors of the human testis. He separated fifty-nine of these tumors from the teratoid group and called them "epithelioma seminal" or "seminome." He considered the various elements in the testis from which they could arise and decided that the most likely structure of origin was the seminiferous tubule. He felt that the spermatogenic elements in the tubule were the ones involved in the process rather than the supporting or Sertoli cells. Bell (1925) regarded the seminoma as a specific tumor of spermatogenic origin. In certain specimens he was able to find histologic characteristics in various tubules adjacent to the tumor which he felt were evidences of hyperplasia. From these tubules he could trace the transition to a gross infiltrating seminoma. He divided seminomas into a subgroup of carcinosarcomas in which he believed that both sarcomatous and carcinomatous elements were blended.

Ewing (1928) believed that seminomas were merely a carcinomatous development in teratomas. He felt that if one sectioned these tumors sufficiently teratomatous structures frequently could be demonstrated. Ewing disagreed with the interpretation that Bell placed on the histologic picture showing the transition from normal tubules to seminoma. Ewing regarded this appearance as either one of benign hyperplasia or actual invasion of the tubules with tumor from the main mass.

Broders (1932) studied the problem of epithelial hyperplasia as opposed to early carcinoma. He stated that "the day has passed when

FIG. 5.

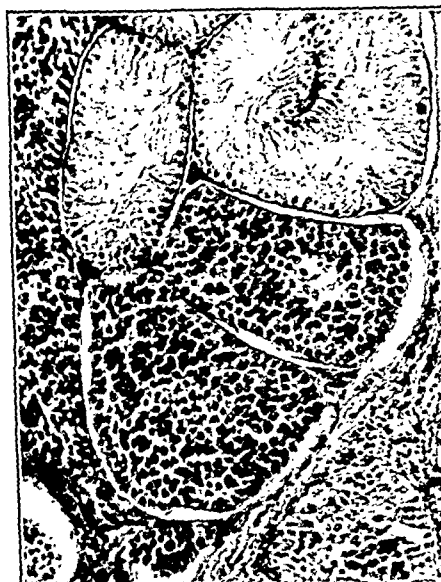


FIG. 7.



FIG. 4.



FIG. 6.



Fig. 4.—Seminoma in the cryptorchid testis of a dog; the multiple foci of origin are shown. The tumor is entirely in situ. The atrophied tubules are contrasted with those filled with tumor cells (hematoxylin and eosin,  $\times 60$ ).

Fig. 5.—Seminoma of testis of a dog; a higher magnification of Fig. 4. The tumor cells are confined to the tubules (hematoxylin and eosin,  $\times 135$ ).

Fig. 6.—Seminoma of testis of a dog; the normal tubules are contrasted with those containing tumor cells which are still in situ (hematoxylin and eosin,  $\times 125$ ).

Fig. 7.—Seminoma of testis of a dog; the tumor is entirely in situ and the tumor cells have an appearance identical with that found in diffuse seminoma (hematoxylin and eosin,  $\times 125$ ).

Fig. 1.

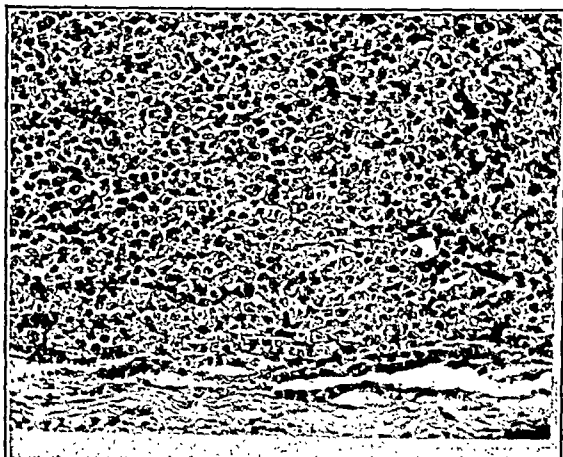


Fig. 2.



Fig. 3.

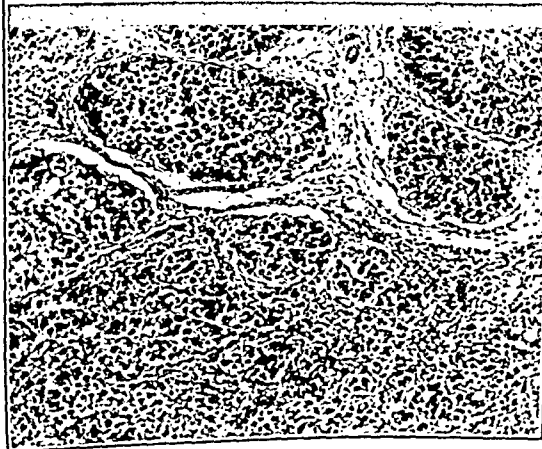


Fig. 1.—Seminoma of testis of a dog, showing marked uniformity in the cellular picture (hematoxylin and eosin,  $\times 205$ ).

Fig. 2.—Seminoma of testis of a dog; the darker areas represent tumor, the multicentric origin being clearly shown (hematoxylin and eosin,  $\times 21\frac{1}{2}$ ).

Fig. 3.—Seminoma in the cryptorchid testis of a dog; a portion of the tumor is still in situ, whereas the remainder is diffuse (hematoxylin and eosin,  $\times 125$ ).

of the seminiferous tubules. This is in agreement with Chevassu's original idea. The objection that such an appearance in the tubules may represent hyperplasia cannot be applicable to this group because the cells in the areas where the seminoma was in situ had a histologic appearance identical to that of metastasis from a seminoma. Furthermore, the idea that these areas of tumor cells within the tubule represented invasion of the tubules from the main tumor cannot be maintained because

Fig. 8.

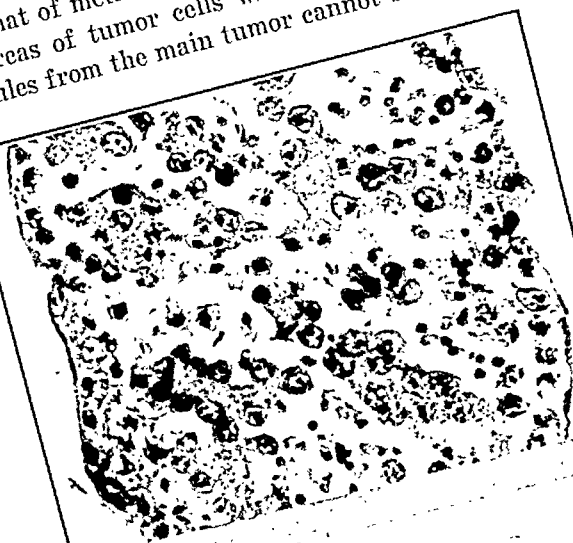


Fig. 9.

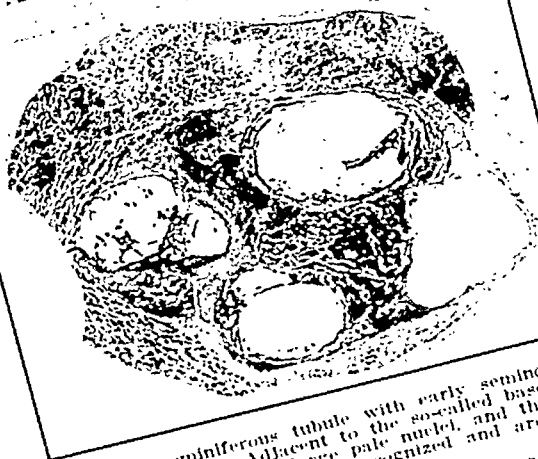


Fig. 8.—Portion of a seminiferous tubule with early seminoma entirely in situ. There are many mitotic figures. Adjacent to the so-called basement membrane, the Sertoli or supporting cells with their large, pale nuclei, and the spermatogonia with their small, deeply stained nuclei, can be recognized and are not involved in the malignant process (hematoxylin and eosin,  $\times 1251$ ).

Fig. 9.—Seminoma associated with an interstitial cell tumor in the testis of a dog. In the center of the testis there is a large interstitial cell tumor which has undergone hemorrhagic degeneration. Around this tumor there is a seminoma which is entirely in situ. The multicentric origin is shown. The paler staining areas represent normal tubules (hematoxylin and eosin,  $\times 31$ ).

in more than one-half of the specimens examined the tumor was entirely in situ. It seems probable that the majority of seminomas originate in multiple foci. When, however, such foci coalesce, it is no longer possible to make such an observation. This was the case in 7 seminomas of this



had not broken through the confines of the so-called basement membrane at any point and so were entirely in situ (Figs. 4-7). In this group the seminomas were in a very early stage of development and had not begun to infiltrate. In the remaining 7 cases, the seminomas were in a much more advanced stage of development and were diffuse. In them the multicentric characteristics, as well as evidence of their origin in the seminiferous tubules, were no longer demonstrable. The cells in the tubules in these cases in which the tumor was in situ were unquestionably malignant; they contained numerous mitotic figures typical of those found in diffuse or metastatic seminoma.

The transition from the normal seminiferous tubule to one filled with malignant cells could be followed in the group of tumors which were still in situ. In the same microscopic field it was possible to find normal tubules adjacent to some which showed early malignant change and to others which were composed entirely of tumor. One early change was the suppression of the formation of spermatids and spermatozoa in the seminiferous tubules. The malignant cells could be traced from the spermatogenic series of cells, apparently the spermatocytes. Normal spermatogonia and Sertoli or sustentacular cells could be demonstrated in many of the tubules in which the seminoma was early and still in situ. The Sertoli or supporting cells could be recognized by their large pale nuclei and prominent nucleoli. The spermatogonia, germinal cells of the spermatocytic series, had smaller nuclei than either the Sertoli cells or spermatocytes, and the nuclei stained very deeply with basic dyes because of clumps of chromatin material (Fig. 8).

Since seminomas originate in the cells of the seminiferous tubules, they are adenocarcinomas or, more specifically, spermatocytomas. All the tumors in this group were highly undifferentiated and were graded 4 according to method of grading tumors used by Broders (1925). Only one seminoma had metastasized. This would emphasize the fact that most of the tumors studied were extremely early.

Seminomas were unassociated with other tumors in 17 instances. Five seminomas were associated only with interstitial cell tumors (Fig. 9); whereas, a seminoma, an interstitial cell tumor, and a grade 1 adenocarcinoma of the so-called Sertoli cell type, were associated in the same testis 3 times.

The average age of the dogs in which seminomas were found was slightly more than 10 years. Most of the testes in which the seminomas were present showed active spermatogenesis. There was, however, no formation of spermatids or spermatozoa in the cryptorchid testes. Two of the scrotal testes in this series presented focal atrophy of the seminiferous tubules.

#### COMMENT

In those specimens in which the tumor was in situ, it was possible to trace the malignant cells directly from the spermatocytic series of cells

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## Erratum

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In the article by Dr. F. Gregory Connell entitled "Partial Gastrectomy in Treatment of Peptic Ulcer," which appeared on page 696 of the May issue, Fig. 1 was printed upside down. It is reprinted here in its proper position.



FIG. 1.—Shift to left in gastric resection

series and is the usual finding in specimens of seminoma of the human testis. When seminomas do become diffuse, with fusion of the various points of origin, it is impossible to demonstrate their origin because they are of such a high grade of malignancy that there is no differentiation into tubules.

It has been shown by various observers that the ectopic testis is more susceptible to the development of tumor than the scrotal testis. This would appear to be true for the dog.

Seminomas were found in animals having an average age of about 10 years. The majority of seminomas in human beings are found between the ages of 35 and 45 years (Chevassu). A comparison of the age incidence of this tumor in human beings and dogs shows that in the dog it occurs in a relatively similar age span. It would appear that seminomas are of relatively more frequent occurrence in dogs than in human beings. However, accurate statistics are not available.

It has been suggested (Peyron, Blanchard, Drieux, and Salomon) that seminomas be divided into the seminal type and Sertoli cell type. To include the latter in the classification does not seem to be justified because Chevassu, in his original description, included only the seminal type. Furthermore, the seminal type usually is of grade 4 malignancy, whereas the Sertoli cell type is almost invariably of grade 1 malignancy. This Sertoli cell type has also been described in the literature as adenoma (Chevassu, Ewing). The four tumors which have been seen in this group are more fully described elsewhere.

#### SUMMARY

Twenty-five seminomas of testes of dogs have been studied. Eighteen of these seminomas were in an early stage of development, being still in situ. In this group it was demonstrated that the tumor arose from multiple foci in the seminiferous tubules. The malignant cells could be traced directly from the spermatogenic series of cells. All the seminomas in this group were regarded as being adenocarcinomas of grade 4 malignancy.

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The recent observations of Goldschmidt, Vars, and Ravdin on the conditioning effect of liver fat on liver necrosis following the administration of volatile anesthetics explain, in part at least, the value of a high carbohydrate diet in patients with serious hepatic disease. The work of Forbes and Neal on the protective action of xanthine against the liver necrosis which follows the administration of chloroform or carbon tetrachloride, while not clearly understood, provides another link in our knowledge of the methods by which protection can be afforded the liver.

It is now generally accepted that the gall bladder is not a vestigial structure, that it does have an important function which is destroyed when it is injured by infection or disease. The contributions of Graham, Cole, Schönheimer, Ivy, Johnston, Riegel, Andrews, and Ravdin have added greatly to our knowledge of normal and pathologic function of this viscus. The investigations of these, and many other workers, have offered more valid explanations of the pathologic physiology of the extrahepatic bile passages and have provided a more reasonable explanation for the persistence of symptoms in patients operated on for gallstone disease.

Less than twenty years ago one of the most brilliant of American surgeons stated that the arterial blood supply of the liver was not necessary for the maintenance of normal hepatic function: "Physiologists point out that the hepatic artery furnishes oxygen to the liver, and this would appear to be true, but the supply is not sufficient to lead us to believe that oxygen is necessary to its function." It is now recognized that the hepatic arterial blood is of the greatest importance in maintaining normal function and that complete ligation of the entire hepatic arterial supply is incompatible with life.

The more recent work on vitamin K and intestinal bile deprivation on the hemorrhagic tendency in obstructive jaundice offers new hope that before long this dreaded complication may be prevented by adequate pre- and postoperative therapy. The alteration in the prothrombin level in obstructive jaundice which has been described by Quick and his associates, and which has now been amply confirmed, provides additional evidence of the important part which fundamental investigations are playing in the better understanding of the problems of the surgical patient.

—*I. S. Ravdin, M.D.*  
Philadelphia, Pa.

# Editorials

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## Recent Advances in Our Knowledge of Biliary Function

THE CONTRIBUTIONS of fundamental science to our knowledge of the physiology and pathologic physiology of the biliary apparatus have had a profound influence on the preoperative preparation and postoperative care of patients with biliary tract disease. The work of Rous and his associates gave new impetus to a study of this system and resulted in a better understanding of the processes involved in disease of the liver and bile passages.

The brilliant researches of Mann and his associates provided new knowledge on the functions of the liver. The important part which this organ plays in carbohydrate, protein, and fat metabolism is being more clearly elucidated. The intermediary metabolism of these food-stuffs, in which the liver plays no insignificant role, is now being elaborated. Only recently the liver has assumed a more important role in the mechanism of production of diabetes mellitus, whether or not one accepts the view that "overproduction" of glucose and fat is the primary factor in this disease. The investigations of Best and his co-workers have added greatly to our knowledge of the liver lipid metabolism.

It is unfortunate, but true, that during this period of intense investigation into the problems of hepatic physiology an attempt has been made to apply the results of these researches to clinical evaluations of hepatic function. In an organ whose known functions require but a small portion of normal liver tissue for their normal activity, the majority of these tests were doomed to failure from the beginning. The carbohydrate metabolism of the liver can be adequately carried on with only 20 per cent of normal tissue, and deamination with even less than this. The dye tests are without doubt of some value and the more recent work of Quick on hippuric acid conjugation has real possibilities. These tests are at present the only methods of real value in clinical practice. When, however, such conditions as anoxemia, anesthesia, hemorrhage, trauma, and infection, which are daily met in surgical practice, can convert a completely normal liver, as determined by the tests now available, into a completely incompetent organ, we must look with prejudice at those tests which give evidence of normal activity of the liver when a major portion of the organ has already been destroyed.

The recent observations of Goldschmidt, Vars, and Ravdin on the conditioning effect of liver fat on liver necrosis following the administration of volatile anesthetics explain, in part at least, the value of a high carbohydrate diet in patients with serious hepatic disease. The work of Forbes and Neal on the protective action of xanthine against the liver necrosis which follows the administration of chloroform or carbon tetrachloride, while not clearly understood, provides another link in our knowledge of the methods by which protection can be afforded the liver.

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Less than twenty years ago one of the most brilliant of American surgeons stated that the arterial blood supply of the liver was not necessary for the maintenance of normal hepatic function: "Physiologists point out that the hepatic artery furnishes oxygen to the liver, and this would appear to be true, but the supply is not sufficient to lead us to believe that oxygen is necessary to its function." It is now recognized that the hepatic arterial blood is of the greatest importance in maintaining normal function and that complete ligation of the entire hepatic arterial supply is incompatible with life.

The more recent work on vitamin K and intestinal bile deprivation on the hemorrhagic tendency in obstructive jaundice offers new hope that before long this dreaded complication may be prevented by adequate pre- and postoperative therapy. The alteration in the prothrombin level in obstructive jaundice which has been described by Quick and his associates, and which has now been amply confirmed, provides additional evidence of the important part which fundamental investigations are playing in the better understanding of the problems of the surgical patient.

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### Continuous Drip Transfusion

**B**ECAUSE the average blood transfusion of 500 c.c. will only raise the hemoglobin from 8 per cent to 10 per cent and is therefore inadequate to cope with the severe anemias, Marriott and Kekwick<sup>1</sup> have recently advocated the use of massive transfusions slowly administered. The method consists essentially of obtaining blood from a number of donors compatible with the recipient and with each other, adding 3.8 per cent citrate solution as an anticoagulant, and permitting its introduction into the vein of the recipient at the rate of approximately 40 drops per minute or 133 c.c. per hour. Because of the tendency of the corpuscles toward sedimentation in the reservoir and the consequent blocking of the drip bulb, a stirring action accomplished by bubbling a continuous stream of filtered oxygen through the blood is necessary. The amount of blood transfused is determined by periodic hemoglobin examinations and the transfusion is discontinued when the normal hemoglobin percentage has been restored.

The advocates of this method contend that it is particularly indicated in that group of cases characterized by severe acute anemia with consequent depression of hematopoietic function in which the ordinary single transfusion of 500 c.c. is of relatively little value. In such cases in which the hemoglobin percentage may be reduced to 25 or 30, it is necessary to administer as much as 4 to 5 liters of blood. Obviously, such massive dosages cannot be given in a single transfusion by the customary procedures. Accordingly, the continuous drip method provides sufficient amounts in such a manner as to obviate possible embarrassment to the cardiovascular system and the development of "speed shock." This latter untoward reaction has been popularized by Hyman and Hirshfeld,<sup>2</sup> who concluded from their investigations that rapid introduction into the blood stream of a great bulk of fluid results in a state of shock.

Whereas it is fully agreed that the customary single transfusion of one pint of blood is merely homeopathic in combating such severe anemias, our discordance with the advocates of this method of transfusion is based on certain fundamental physiologic principles. It is inopportune here to enter into a lengthy discussion of the pros and cons of the citrate method of transfusion, but our opinion is succinctly and aptly expressed in the words of Lederer,<sup>3</sup> who states: "The general principle that the more closely the blood introduced into the recipient approximates the blood in its natural condition is a fundamental one. No matter how simple and how easy a method is, if that method permits of changes in the blood due to the admixture of foreign substances, to changes in reaction or temperature, to biological alterations in morphology (coagulation), and to ferment action, it is a departure from this principle." Aside from this rational disadvan-

tage of the continuous drip method, the same therapeutic effects can be accomplished more physiologically and more simply by frequently repeated transfusions of unmodified blood. We have often transfused as much as 5 to 7 liters of unmodified blood in three or four days. Moreover, there has never been any untoward reactions in these cases. As regards the phenomenon of "speed shock," our experience has been similar to that of Milbert<sup>4</sup> and Unger.<sup>5</sup> In well over 5,000 transfusions this reaction has never been observed, and not infrequently as much as 650 c.c. is transfused in three minutes.

Thus, because in our experience the same purpose and advantages claimed for continuous drip transfusion can be obtained by frequently repeated transfusions of unmodified blood and because this latter method is more rational, more physiologically ideal, considerably simpler, and certainly as safe or safer, we find the indications for the continuous drip procedure conspicuously restricted.

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# Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

## MAMMARY TUMORS

CHARLES F. GESCHICKTER, M.D., BALTIMORE, MD.

(From the Surgical Pathological Laboratory, Department of Surgery, Johns Hopkins Hospital and University)

IT IS generally stated that a lump found in the breast of a woman who has reached or who has passed sexual maturity is presumably cancer until proved otherwise. Since the mammary gland is frequently the seat of hyperplastic changes and benign tumor formation, this assumption increases the importance but does not simplify the problem of differential diagnosis. The presence of multiple lumps in the breast of women with chronic cystic mastitis during the childbearing period, the appearance of a solitary nodular growth in the postpuberty period, in cases of fibroadenoma, and the occurrence of a nodule near the nipple associated with a sanguineous discharge in cases of intracystic papilloma are relatively common. Together these cases of chronic cystic mastitis, fibroadenoma, and intracystic papilloma are about as frequent as carcinoma. The clinical and pathologic features which aid in distinguishing these benign lesions from carcinoma have become increasingly important, since the campaign of public education in regard to cancer is bringing patients for examination at a stage when the classical symptoms and signs of carcinoma are lacking.

### HYPERTROPHY AND HYPERPLASIA

*Hypertrophy of the Mammary Gland.*—Hypertrophy of one or both breasts occurs in both males and females and is more easily distinguished from carcinoma (because of the diffuse enlargement of the gland) than mammary hyperplasia in chronic cystic mastitis, which results in the formation of one or more nodules. Enlargement of the breasts in female infants, accompanied at times by menstruation, is found in cases of sexual precocity. The most common cause of such instances of infantile mammary hypertrophy is a granulosa cell tumor of the ovary. Rarely, the precocity may be produced by a pituitary disturbance and anterior pituitary-like hormone in the form of prolactin can be demonstrated in the urine. In such cases the pituitary activity stimulates the formation of follicular cysts in the ovary lined by granulosa and theca lutein cells which secrete estrin and bring about the

mammary development. In the cases of granulosa cell tumor an increased secretion of estrin is also responsible for the abnormal growth of the breast. That hypersecretion of estrin may be the causative factor is suggested by the production in girls of infantile hypertrophy after the injection of this hormone when it is used in the treatment of gonorrheal vaginitis (Fig. 1).

In girls at puberty breast development may greatly exceed the normal in one or both breasts. Asymmetrical enlargement of the breasts between the ages of 10 and 13 years usually corrects itself by the end of puberty. In cases where the enlargement continues to abnormal size, the exaggerated breast development is the result of excessive



Fig. 1.—Infantile hypertrophy of the breast, in a girl aged 2 years. The patient had been menstruating since the age of 3 months and had both pubic and axillary hair and a positive Aschheim-Zondek test in the urine. The condition was apparently produced by overactivity of the anterior lobe of the pituitary.

amounts of duct and periductal tissue similar in other respects to that found in normal puberty. There are thirty-three such cases recorded in this laboratory. In these cases there is apparently an increase in the blood level of estrin and an increased susceptibility of the breast to this ovarian secretion. Virginal hypertrophy once established tends to persist (Fig. 2). To date we have had no encouraging results from endocrine therapy, and surgery is indicated where the enlargement is excessive. In about one-tenth of the cases a localized fibroadenoma will be found in one of the enlarged breasts. This occurred in a patient reported by Johnson and Bloodgood in 1906. Enlargement of the breasts approaching virginal hypertrophy and known as gravid hyper-

trophy may be seen in women who have borne their first child, persisting after lactation but having its onset during pregnancy.

*Gynecomastia.*—Gynecomastia in the male is the homologue of virginal hypertrophy in the female (Fig. 3). Slight and transient enlargement of the breast at puberty is a normal occurrence in a definite percentage of males. Jung and Shafton found temporary enlargement in 36 per cent of boys between 12 and 13 years and in 77 per cent between 13 and 14 years. One or both breasts may be diffusely enlarged and the condition persistent, either at puberty or with the decline of sexual life. The benign enlargement, as in infantile or virginal hypertrophy in the female, is the result of increase in the length of ducts and in periductal connective tissue. Clinical observations indicate a definite relationship

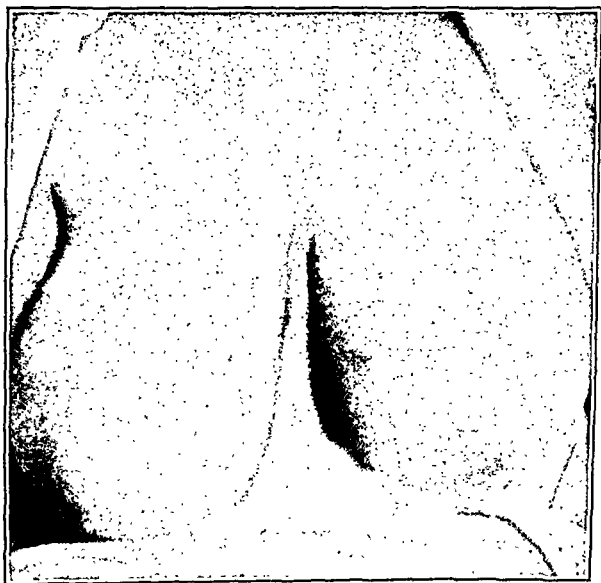


Fig. 2.—Virginal hypertrophy beginning at the age of 13 years before the onset of menstruation. These breasts are unusually sensitive to estrin stimulation.

between the sex organs and gynecomastia (Lewis and Geschickter). Enlargement of the male breast is observed in hermaphrodites. This condition occurs in 5 per cent of the cases of chorioepithelioma or teratomas of the testicle (Ferguson). In boys or young adults excision or atrophy of one testicle with hypertrophy of the interstitial cells of the opposite testicle may lead to mammary enlargement. Mochling has reported cases of hypophyseal tumors in men with enlargement of the breast. The chorionic tissue present in testicular tumors has been found to secrete both prolactin, the pituitary-like sex hormone, and estrin, the female sex hormone. Injections of estrin alone will produce this gynecomastia in male monkeys and in humans. Apparently, therefore, the indirect action of the anterior pituitary hormone and the direct ac-

tion of estrogens are the etiologic factors. Mammary enlargement of the male is usually self-limited and benign. A period of observation should elapse to determine whether the condition will regress spontaneously. Once established, it does not respond to endocrine therapy. Excision is indicated for cosmetic reasons.

#### SUBINVOLUTION AND HYPERPLASIA OF THE MAMMARY GLAND

The term chronic cystic mastitis is loosely applied to a group of benign conditions of the breast. Painful breasts and nodular hyperplasia (so-called adenosis or Schimmelbusch's disease) are included under this term. A separate group of cases occurring toward the menopause,

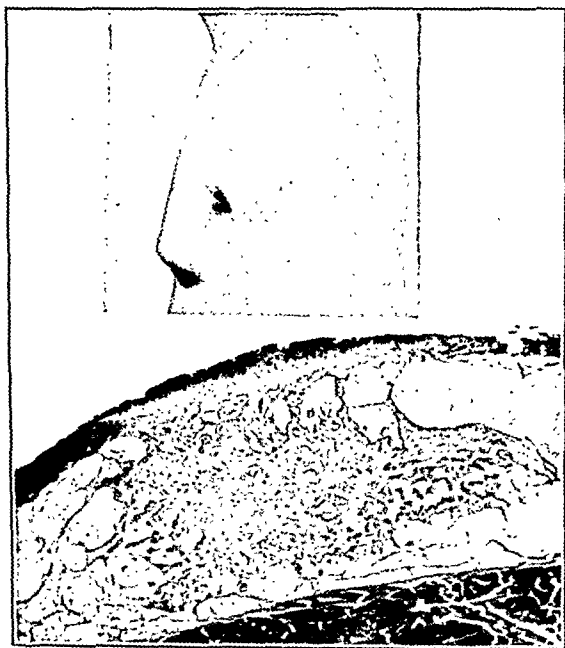


FIG. 3.—Photograph of patient and cross section of the breast, in a case of gynecomastia occurring in a boy aged 18 years.

characterized by cysts of appreciable size and related to abnormal involution of the mammary gland, is also included. With the approach of the menopause or following abnormally high and prolonged estrogenic stimulation, involutional changes occur in the mammary ducts. The epithelial ramifications of the terminal tubules, which form the mammary lobules so characteristic of the normal breast in the child-bearing period, atrophy and disappear. The ends of the remaining branches of the ducts dilate and their lining cells secrete. In this phase of involution simple cysts may occur.

*Cystic Disease.*—Cystic disease is characterized by the development within the breast of one or more cysts of appreciable size. Several cysts may develop over a period of several years in the same patient.

but usually when the patient is first examined there is but one cyst. Cystic disease occurs more frequently in women who have not borne children. In the present series of 580 cases, the cysts, in 80 per cent of the cases, occurred in the forties, or near the menopause. The women affected had regular menstrual cycles and were apparently healthy in other respects. Premenstrual pain or indurated areas in the breast are unusual. Cysts make their appearance abruptly. The known duration

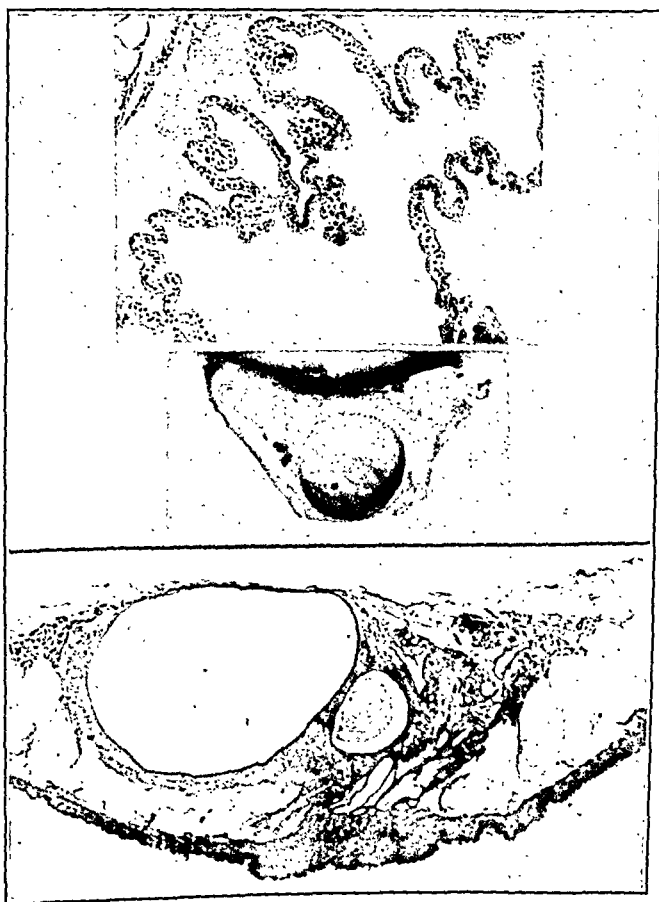


Fig. 4.—Cross section of the breast, gross specimen, and photomicrograph of epithelial lining in cystic disease.

of the tumor is often given in days or weeks rather than in months or years. The breasts affected are well developed and contain increased amounts of fatty or fibrous tissue. The cyst is round, smooth, and freely movable. It transilluminates clearly and upon aspiration cloudy milk-like fluid is obtained. (Fig. 4.) When one or more cysts have appeared and spontaneously disappeared, a residual area of fibrosis may remain. Successive cysts involved both breasts in 17 per cent of the cases. Rarely,

as described by Reclus, multiple cysts of appreciable size may be present at the same time in both breasts. A form of cyst resembling a galactocoele may form in a pre-existing fibroadenoma during lactation.

The diagnosis of a cyst may be confirmed by aspiration of the cloudy milk-like contents, and this often suffices for treatment. Following aspiration, injections of estrin (10,000 international units) twice weekly for two months will control the condition in some cases (Lewis and Geschickter). The injections should be halved in number the following month and further decreased in the next month. If there is any doubt concerning the diagnosis, excision should be performed. Cysts with bloody contents or with papilloma in their walls may contain cancer.

*Mammary Hyperplasia—Painful Breasts.*—A frequent precursor of the lesion that may develop into the hyperplastic form of cystic mastitis or adenosis is the painful breast. This condition is characterized by cyclic pain, which reaches its maximum intensity before the menstrual period. Three hundred and seventy-five cases have been studied. In the early stages the painful and tender tissue is usually in the upper and outer quadrants and feels like a flat, granular area of increased density. Menstruation is usually regular; the patient is in her thirties and either is childless or has not been pregnant for five or more years. In married women with this complaint there is a high percentage of sterility. Mammary pain and tenderness, which are premenstrual in the early stages, become more severe and are prolonged throughout the entire cycle. Fear of cancer is often aroused. An area of increased density may be palpated in the breast. These patients are usually not undernourished and are not of the nervous type. The granular or nodular areas of increased density, which at first vary at different periods of the menstrual cycle, may persist. Spontaneous regression may occur, but often adenosis and less frequently cystic disease supervene after a period of months or years.

This early stage of chronic cystic mastitis characterized by persistent painful breasts may be successfully treated by endocrine therapy (usually estrogen administered intramuscularly twice a week in doses of 10,000 international units over a period of several months as described above for cystic disease). The indurated tender mammary tissue palpated in the outer upper quadrant usually of both breasts in these cases is readily distinguished from the well-defined hard nodule of carcinoma.

*Adenosis, Schimmelbusch's Disease, or the Proliferating Form of Chronic Cystic Mastitis.*—In married women who have not borne children for five or more years or in childless or unmarried women, painful, shotty masses may develop in the outer, upper quadrants of one or both breasts after the age of 35 years. Many of these women have suffered with painful breasts during the premenstruum for a number of years. As the condition progresses, the stroma of the breast is increased in density and the size of the breast is reduced. The breast

has a saucer-like or liver-like edge. Pain, flat areas of increased density and numerous indefinite nodules are present, but in addition discrete multiple tumors may be palpated, which histologically may prove to be small papillomas, minute cysts, or nonencapsulated adenomatous areas. (Fig. 5.) The 175 patients with typical adenosis in the present study were in the late thirties or early forties with few exceptions. Menstruation is apt to be painful or irregular or the cycle shortened to

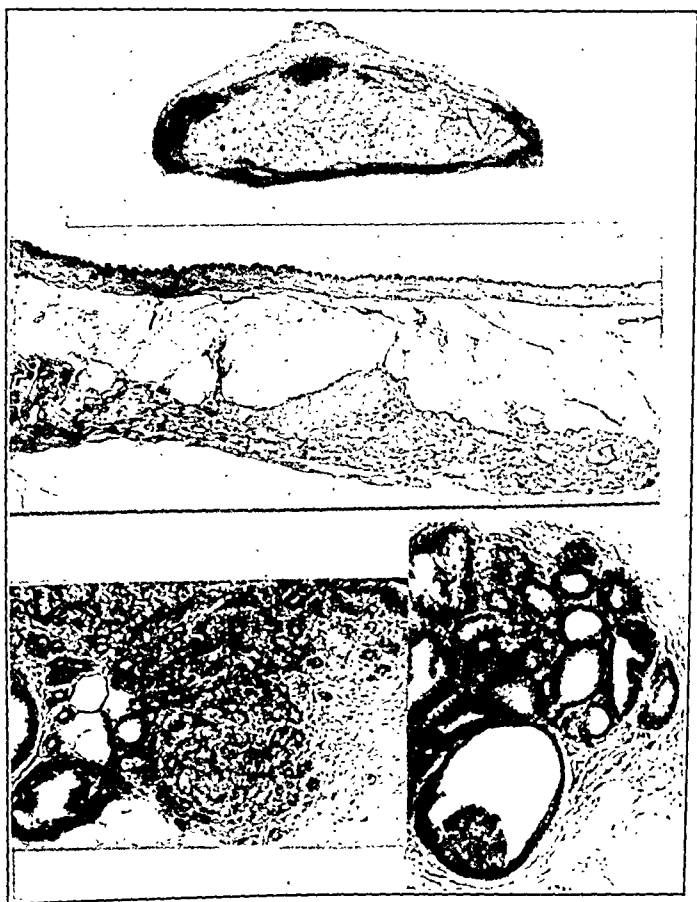


Fig. 5.—Gross specimen, cross section, and photomicrographs in adenosis or Schimmelbusch's disease. The hyperplastic tissue contains small cysts, minute intracystic papillomas, and nonencapsulated epithelial proliferation.

twenty-six days or less. Pregnancy or the menopause may cause these changes to disappear. In rare instances a benign papilloma or a comedo carcinoma develops. Usually, however, the condition is self-limited and terminates with the formation of multiple small cysts. Spontaneous return of the breast to normal before the menopause is rare, occurring in less than 5 per cent of our series. The patients are usually highstrung, nervous, and underweight. The thyroid gland is moderately enlarged.

Since the condition is bilateral and diffuse, local excision is inadequate therapy. Such excision, however, for purposes of biopsy may be performed where a single nodule, more definite and larger than the others, develops. In our opinion mastectomy is not indicated. These cases show marked improvement on estrogenic therapy beginning with doses of 10,000 international units twice weekly for two months and gradually decreasing by half the number of doses in the succeeding months. Fibrosis or the formation of small cysts may result from such treatment. Many authors believe that this condition is precancerous. In the present series of 533 cases we were able to follow 271 patients for over five years. In only 3 of these carcinoma of the breast developed, an incidence of less than 2 per cent.

Experimental evidence indicates that cystic disease and mammary hyperplasia or adenosis are the result of disturbances in the hormonal physiology of the breast. Large cysts of the mammary gland can be produced in the rat breast by brief, intense stimulation with estrin. In such experiments abnormal epithelial buds replace normal lobule development in the terminal tubules, following injections of large doses of estrin. With further dosage these epithelial masses in the terminal tubules undergo maturation and secretory activity leading to cyst formation. If, instead of estrin, hormones are injected which normally produce lobule development in the rat breast (testosterone), atypical epithelial proliferation with small cysts occurs in the terminal tubules, producing a histologic picture similar to that seen in adenosis.

#### BENIGN TUMORS

*Benign Papilloma.*—Hyperplastic epithelium in adenosis is accompanied by the formation of multiple small intracystic masses of basal cells which occasionally take the form of minute papillomas. These rarely exceed the size of a fraction of a millimeter. They tend to regress spontaneously with the menopause. The clinical condition spoken of as intracystic papilloma refers to a tumor of macroscopic size, usually 2 or more cm. in diameter which occurs usually in the region of the nipple or midzone of the breast in women near the menopause. (Fig. 6.) Approximately 50 per cent of these lesions are accompanied by a bloody discharge from the nipple. The tumor is usually palpated near the nipple zone, is soft, or smooth and tense, and is freely movable. It may occur in the ampullae of the nipple itself. The tumor casts a dark shadow upon transillumination.

In 160 benign intracystic papillomas in the present study, the majority had been noted by the patient for two years or more prior to examination. The average diameter of these growths was 3.1 cm. The majority of the cases were 1 to 2 cm. but among cases observed in earlier years 35 were 6 cm. or over. Ninety-five per cent of the tumors were beneath the nipple or in the midzone. Although the peak of age incidence was between 40 and 45 years, the youngest of the patients affected was 15 and the eldest 74. Tumor and serous or sanguineous discharge from the



nipple were the leading symptoms. Variation in size of the tumor following rupture of the cyst and bleeding from the nipple was noted in 6 cases. The tumor on palpation was soft, cystic, or firmly nodular, according to the notes in the history. The nipple was either normal, slightly retracted, or protruded on examination. Fixation did not occur except in the 2 instances where infection had complicated the growth.

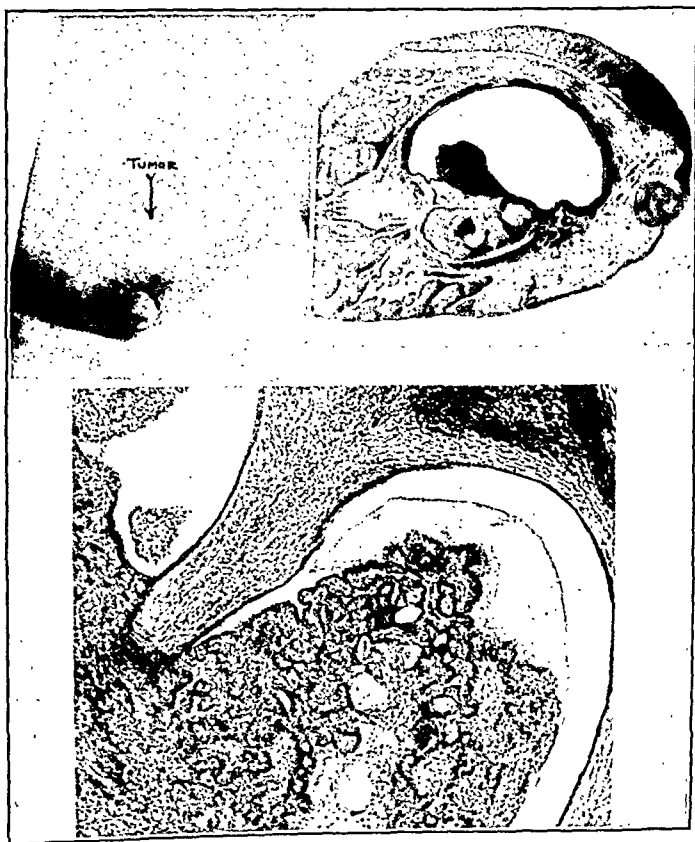


Fig. 6.—Photograph of the patient, the gross specimen, and photomicrograph of benign intracystic papilloma. The tumor is near the nipple and in the gross and under the microscope is completely encapsulated.

On pathologic examination a cyst containing bloody fluid and a soft papillomatous mass are found. In 38 per cent of the cases multiple papillary growths were found pathologically and in 15 per cent of the cases a sanguineous discharge or similar tumor was noted clinically in the opposite breast, either at first or subsequent examination.

Microscopically the tumor consisted of branched stalks of fibrous tissue, overlaid by orderly rows of columnar or oval epithelium. Despite the fact that pathologic study indicates that a certain percentage of these tumors undergo malignant change, simple excision usually suffices to cure.

Forty patients in the present series were treated by the radical operation for cancer. Thirty-eight patients had a simple mastectomy performed, 4 of these having both breasts removed. One had, in addition, excision of a similar tumor from the opposite breast. In all, 82 breasts were amputated for benign intracystic papilloma, 40 of these receiving, in addition, axillary dissection. Up until 1925 only 22 cases were treated by simple excision. This number has been increased to 65 at the time of the present writing. Of these, 6 had two or three excisions.

In this series the radical or simple amputation of the breast was performed for two reasons: First, because the gross or microscopic appearance of the tumor suggested malignancy. In the majority of cases when the radical operation for cancer was performed in the older cases, it was based upon the finding of bloody contents in a cystic tumor at exploration, a finding which was formerly held to indicate the presence of cancer. Second, it was performed because of the opinion formerly held in this clinic and still maintained by many surgeons and pathologists that a sufficient number of these tumors undergo malignant change to justify radical treatment in all cases. This rule is also applied by some in patients having a sanguineous discharge from the nipple without a demonstrable tumor. Twelve of the patients in this series were treated with wide excision of the nipple and breast tissue or by amputation of the breast because of a bloody discharge from the nipple, although no tumor could be demonstrated on examination prior to operation.

A sufficient number of cases treated by simple excision have now been followed to justify the conclusion that benign intracystic papilloma can be treated safely by simple excision. The excised tumor should be subjected to microscopic examination and, if the epithelial contents of the cyst show no evidence of malignancy, no further treatment is indicated. Invasion of the neighboring ducts outside of the capsule of the tumor by epithelium similar to that found in the tumor but without definite papillary formation is the earliest sign of malignant change in our experience. The radical operation should be performed in such cases.

*Fibroadenomas.*—Fibroadenomas are benign, well-encapsulated tumors, found most commonly following puberty. In 600 cases studied, the peak of age incidence was between 20 and 25 years. The tumors grow slowly, the duration averaging from 3 to 4 years.

In fibroadenomas there is an increase in duct epithelium, periductal and perilobular connective tissue. In many instances no acinar formation is noted, as in virginal hypertrophy and gynecomastia.

Solitary fibroadenomas are most frequently noted in the upper and outer quadrant of the breast at the periphery. On palpation they have a lobulated, elastic feeling and are freely movable. In one-third of the cases the nodule is painful or tender. Rarely does the nodule increase in size during menstruation. Increase in size, however, is the

rule during pregnancy. The breast containing the fibroadenoma or fibroadenomas is usually well developed (Fig. 7). Local excision suffices to cure in these cases, but in about 10 per cent of the cases in which local removal has been performed similar growths have developed subsequently.

Women near the menopause who are treated for this type of tumor usually give a long history when carefully questioned, and at this time

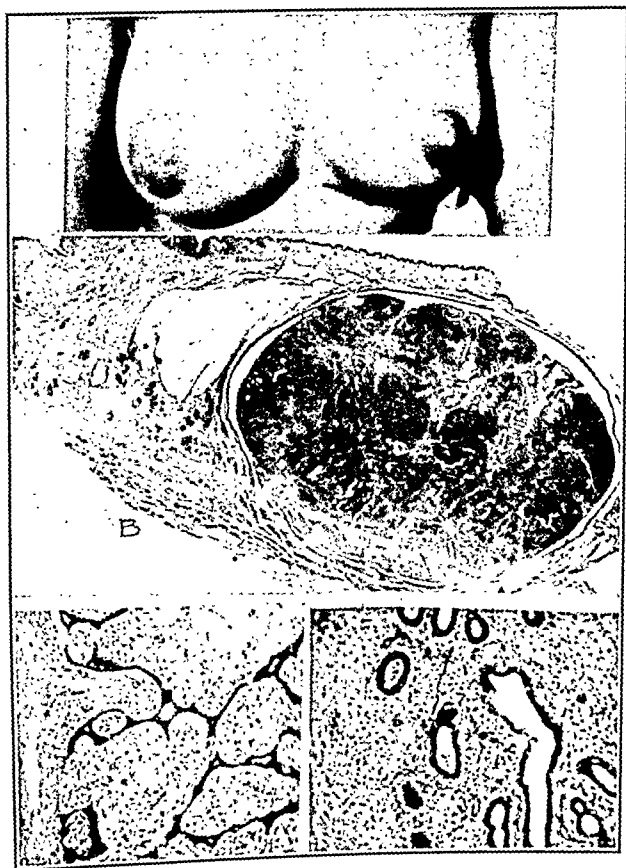


Fig. 7.—Photograph of the patient, cross section of the breast, and photomicrograph in a case of fibroadenoma. The encapsulated character of the tumor is well shown. The photomicrograph on the left shows a myxomatous portion of the tumor; that on the right is typical fibroadenoma.

of life renewed growth energy in the tumor may be noted. In such cases the tumor not infrequently has the histologic appearance of an intracanalicular myxoma, with large amounts of loose embryonic connective tissue surrounding the epithelial structures. In the quiescent cases of long duration a more adult stroma is found. The difference in type of the connective tissue is related to the rapidity of growth and is usually the only distinguishing feature between fibroadenomas and so-called intracanalicular myxomas. In fibroadenomas of long

standing, dilated ducts and small cysts occur. These are sometimes referred to as cystic adenomas. In general, rapid growth of fibroadenomas is incompatible with regular menstruation. Growth of the tumor is therefore most frequently encountered at puberty, in pregnancy, or with the menopause. With repeated menstruation or lactation, the tumor tends to undergo cystic and regressive changes.

*Fibrosarcoma.*—Rapidly growing intracanalicular myxomas in women beyond the childbearing period are often considered malignant be-

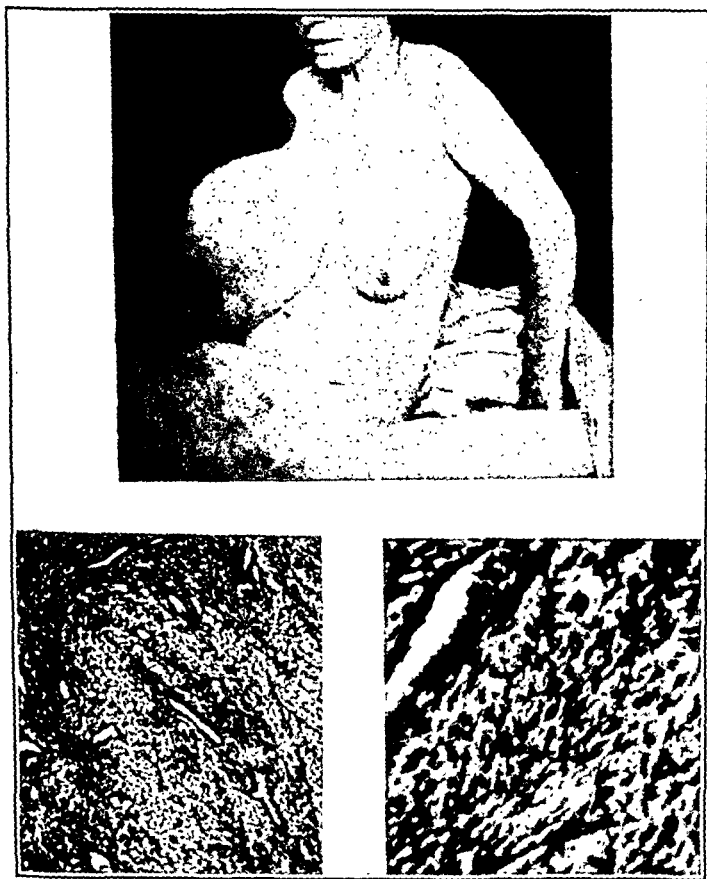


Fig. 8.—Photograph of the patient and low and high power photomicrographs in a case of fibrosarcoma. Many of these cases are rapidly growing fibroadenomas but a few metastasize.

cause of their size, hardness, and nodularity. The majority of the lesions retain their benign character. Fibrosarcoma, however, usually of low malignancy, with invasion of the pectoral muscle but not the axillary nodes, may supervene (Fig. 8). Most of these can be related to preexisting fibroadenomas on the basis of the clinical and microscopic findings. There were 49 such cases in the present series. Usually the malignant tumor develops at the site of a fibroadenoma of many years' duration, the period of rapid growth extending over 3 to 5 years.

Microscopically all gradations can be found from markedly cellular stroma without sarcomatous features, to rapidly growing sarcoma of the spindle-cell type. Because of the tendency for these sarcomas to invade the underlying musculature rather than to metastasize by the lymphatics, an amputation of the breast with the pectoral muscles, but without an axillary dissection, should be performed. In cases treated by simple excision recurrence may result. Nine of the cases of fibrosarcoma in the group of 49 cases studied died of metastases.

#### CANCER OF THE BREAST

Mammary carcinoma ranks third in cancer mortality tables, being exceeded only by cancer of the stomach and uterus. The present-day curability of all forms of mammary cancer by radical surgery is variably stated, the figures usually ranging between 30 and 40 per cent. Attempts have been made to increase the number of cures in three ways: by education of the public and profession to secure earlier diagnosis and treatment; by combining irradiation and surgery; and by preventive measures directed against certain alleged precancerous lesions of the breast.

An analysis of 2,300 cases of cancer of the breast treated over a period of fifty years (1889 to 1938) at the Surgical Clinic of the Johns Hopkins Hospital shows that the curability of breast cancer varies with the pathologic type as well as with the stage of the disease. It indicates a 5 per cent increase in the curability of all forms of mammary cancer in the last two decades as a result of the educational campaign.

*Infiltrating Adenocarcinoma or Scirrhus Mammary Cancer.*—Approximately three-fourths of all mammary carcinomas arise from the glandular epithelium of the terminal tubules. This common variety of adenocarcinoma, variously termed gland cell or scirrhus cancer, is seen clinically in four different forms.

It occurs usually as a tumor, 1 to 5 cm. in diameter with atrophy of the overlying fat and with or without retraction of the skin or nipple. It may occur as a large mass occupying one or more quadrants of the breast. In other cases one or more recurrent nodules are found in the scar of a preceding operation. In a small group of patients a relatively small tumor with extensive skin involvement, so-called acute or inflammatory cancer, is found. (Fig. 9.)

The usual form of scirrhus cancer is a small hard mass, 1 to 3 cm. in diameter occurring at or near the menopause in a woman who has

CLINICAL TYPES OF INFILTRATING (SCIRRHUS) CARCINOMA OF THE BREAST

TYPE	CHARACTER OF TUMOR	NO. OF CASES	FIVE-YEAR SURVIVALS
1. Small infiltrating cancer	1 to 5 cm. in size	1050	29%
2. Large infiltrating cancer	6 to 14 cm. in size	420	5%
3. Recurrent cancer	One or several nodules	220	7%
4. Acute or inflammatory cancer	Extensive skin involvement	20	0%

borne one or more children. The majority of the cases occur between the ages of 40 and 55 years. The patients have noticed the presence of a lump or nodule six months or less prior to the time of examination.

The clinical history and findings in the ordinary form of small infiltrating mammary carcinoma under discussion are remarkably uniform. The four major findings on the examination of the breasts are: first, the presence of a single lump in a breast otherwise normal to palpation; second, the hardness and irregularity of the tumor to palpation; third, the apparent nearness of the tumor to the examining finger be-

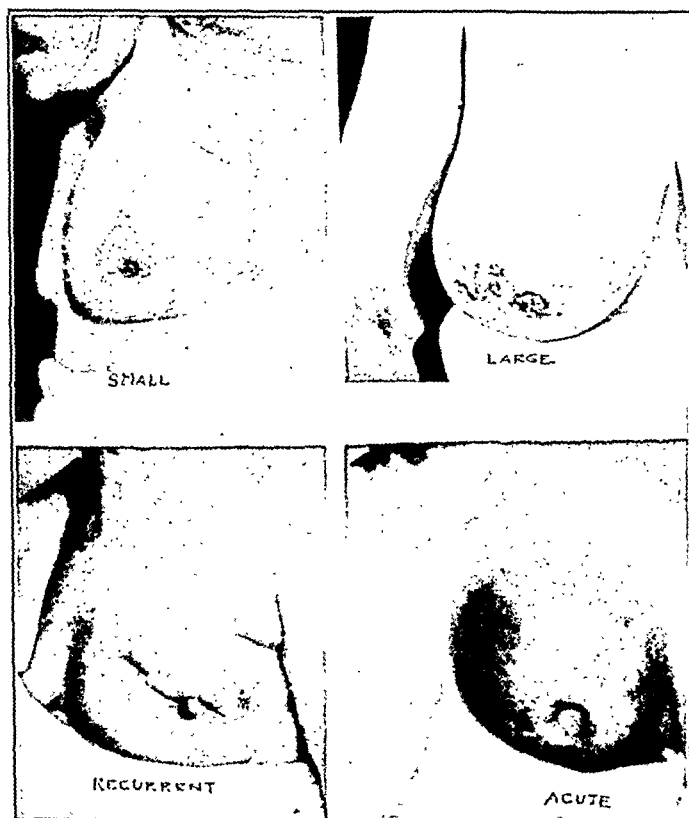


FIG. 3.—Photographs of patients with small, large, recurrent, and acute forms of infiltrating adenocarcinoma (scirrhous cancer).

cause of atrophy of the overlying fat; and fourth, retraction of the skin or nipple indicated in their earliest phases by dimpling of the skin or a difference in the position of the nipple on the affected side when the patient in the erect position slowly elevates her arms. Discharge from the nipple is not a common symptom in this group and was noted only 26 times in the series of 1,050 cases.

Pathologic findings are as uniform as those observed clinically. The tumor on section is usually a dense whitish yellow stellate mass which is gritty and its surface retracts or "cups" when cut through with a knife.

Small secondary masses may be found in the neighborhood of the main growth or the tumor may be elongated and may extend toward the nipple or toward the periphery of one of the quadrants of the breast. The surrounding breast is usually fatty with traversing bands of fibrous tissue and poor in parenchymatous tissue. The tumor most frequently is found in the outer and upper quadrants or in the upper inner quadrants of the breast, but it may occur in any of the various quadrants or in the central zone.

On microscopic examination the tumor cells are of moderate size with moderate amounts of cytoplasm with vesicular nuclei which contain distinct nucleoli and occasional mitotic figures. The cells grow characteristically in small nests or islands or narrow elongated cords with large amounts of intervening fibrous tissue and small amounts of lymphoid infiltration. In the more slowly growing tumors the cancer cells are dispersed by large amounts of fibrous tissue or form acinar or tubular structures. (Fig. 10.)

Although the more unfavorable cases of scirrhus carcinoma, including those exceeding 5 cm. in diameter, recurrences following incomplete removal, and acute carcinoma, have been excluded from the group of small infiltrating scirrhus cancer, the results following radical surgery show that only 30 per cent of the patients survived the five-year period. These results are in keeping with those of Hutchinson who collected figures from fifty clinics and found the surgical results showed 28.1 per cent of five-year survivals.

While this group of small infiltrating cancers represents only one-half of the entire series of mammary cancers, the percentage of five-year cures is fairly representative of the entire group. This is true because the remaining half is about equally divided between large advanced or hopeless cancers in which the percentage of cures is 7 per cent and low grade cancers including carcinoma secondary to benign papilloma, to chronic cystic mastitis and gelatinous carcinoma in which the cures average 61 per cent.

*Large Infiltrating Scirrhus Carcinoma.*—In 420 cases in the present series the tumor measured 5.5 cm. or more in diameter. These cases were similar in other respects and belonged microscopically to the same group as small infiltrating scirrhus carcinoma. This group of cancers is characterized by a diameter greater than 5 cm., by their hard nodular character on palpation, and by their adherence to the overlying skin, with or without ulceration. They have been grouped separately because of their extremely unfavorable prognosis. With but four exceptions, metastasis to the axillary glands had occurred prior to treatment and only 8 cases survived the five-year period. A study of this group demonstrates that a scirrhus cancer (recognized on palpation by its hard and fixed character) which has reached a size of more than 5 cm. in its greatest diameter is incurable by radical surgery. Irradiation or some other form of palliative therapy (simple mastectomy) is indicated.

Except for their longer duration and a younger average age, the symptoms of large infiltrating scirrhus carcinoma resemble those found in smaller tumors of the same type. A higher percentage noted pain or tenderness prior to examination and had not sought treatment previously because the lump had not caused pain or discomfort. One-fourth of

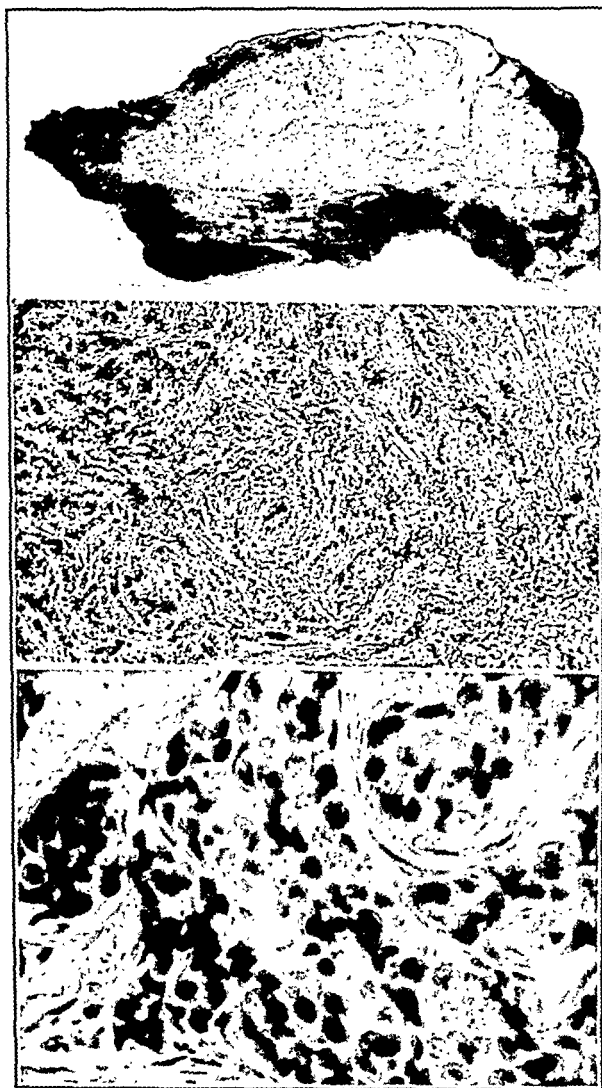


Fig. 10.—Gross specimen, and low and high power photomicrographs of infiltrating (scirrhus) adenocarcinoma.

the cases had noted that the overlying skin had become "angry" or ulcerated and mentioned this as a reason for seeking treatment. (Fig. 11.)

This group of cases presented all the classical signs of cancer of the breast emphasized in the older literature. The tumors occupied one or



more quadrants of the breast. They were hard and fixed to the overlying skin and sometimes to the underlying muscles. Discoloration, edema with "orange peel appearance" secondary nodules in the skin, ulceration, and fungating tumors were among the skin changes noted. Enlarged axillary nodes were noted with few exceptions in the histories and microscopically they contained metastases in all but 4 cases. Discharge from the nipple was noted in 3 per cent of the cases and was described as bloody, foul, or pus. To this group belongs the greatest number of cancers which ultimately involved both breasts. In 12 of the pa-



Fig. 11.—Photomicrograph of patient and gross specimen illustrating an advanced case of large infiltrating scirrhus cancer.

tients both breasts were apparently involved at the time of first admission, the bilateral amputation being done in 2 on the first admission and in the remaining 10 with an interval of about one month between the removal of right and left breasts.

These cases are remarkable pathologically for the absence of necrosis and softening in the tumor in spite of its size. In a few instances secondary infection entering via the pathway of the nipple and larger ducts caused areas of degeneration and necrosis. In many instances the tumor was infiltrated throughout the mammary tissue. In other cases

two or more large masses with adjoining surfaces or connected by infiltrating strands of tumor were found on section. Microscopically these large tumors do not differ from the smaller scirrhus cancers.

All of the cases in the present series of large infiltrating scirrhus cancers were treated surgically, although some of the recent cases had pre- or postoperative irradiation. In the earlier decades many received radical Halsted operations, though in some instances the supraclavicular and axillary regions were dissected after an interval of days or weeks following the amputation of the breasts with the pectoral muscles. In the more recent cases the larger tumors with ulceration or skin involvement were treated by simple amputation of the breast including the pectoral muscle in combination with irradiation with no attempt to perform the axillary dissection. Although this group of cases is inoperable according to modern standards, 8 cases survived the five-year period.

*Recurrent Cancer.*—In 220 cases of mammary cancer in the present series radical operation was performed for recurrence after incomplete operation or dissections were performed for recurrent masses following a previous complete operation for cancer. In this group of cases there are many who had repeated operations for recurrences. One patient had a complete operation in December, 1921, and had twenty local operations for recurrences, finally dying in July, 1928, supposedly from pneumonia. In a similar case the tumor was first excised in 1926, the radical operation was done in 1929, and two local operations done for recurrence in 1930, the patient ultimately dying in 1933. Usually the local recurrence appeared within 1 to 2 years following the complete operation, or sooner if an incomplete operation was performed. There are 14 cases, however, in which the local recurrence took place 5 or more years after the complete operation. In one case the first recurrence was 20 years after the complete operation, in one case 12 years after, and in three cases, ten years after the complete operation. In all there were 28 cases in which both breasts were ultimately involved. With the exception of 4 cases, these patients did not survive the five-year period, following the appearance of the recurrence.

In a small group of cases known as acute or inflammatory carcinoma skin metastases appear before a nodule of appreciable size is discovered in the breast. Fortunately this type of carcinoma with early skin manifestations (sometimes spoken of as erysipeloid cancer) is rare and occurs only 20 times in the present series. There were no five-year survivals in this group, although palliative results were obtained with deep x-ray therapy.

#### CIRCUMSCRIBED FORMS OF MAMMARY CANCER

One-fifth of the cases of mammary carcinoma in the present series differed clinically and on gross examination from the more common variety of scirrhus cancer. Microscopically, this smaller group includes

carcinoma secondary to benign papilloma, gelatinous or mucoid cancers, and comedo carcinoma growing in the mammary ducts. They are characterized by a slower growth and a better prognosis (there are 61 per cent of five-year survivals). Clinically these tumors are distinguished by their softness on palpation and by their circumscribed form.

CIRCUMSCRIBED FORMS OF MAMMARY CANCER

TYPE	CHARACTER	NUMBER	FIVE-YEAR SURVIVALS
Papillary adenocarcinoma	5 to 6 cm., soft, circumscribed	260	60%
Gelatinous cancer	4½ cm., long duration, cystic	75	58%
Comedo carcinoma	localized or diffuse	135	67%

*Papillary Cancer.*—The majority of the circumscribed forms of mammary cancer show a papillary structure, both in the gross and under the microscope (Fig. 12.) They are often of large size and of more than a year's duration. The central portion of the breast near or beneath the nipple was affected in one-sixth of the cases in this series and a sanguineous discharge from the nipple occurred in 10 per cent. The growth differs from scirrhus cancer, being softer to palpation and remaining in many instances freely movable despite its size. Distant metastases occur late and local recurrence or involvement of the other breast often precedes metastases to the internal organs. Thirty per cent of these cases occurred in the colored race; whereas, in other forms of cancer slightly over 20 per cent were affected.

In the present series there were 260 cases of papillary carcinoma. The average size of these tumors is between 5 and 6 cm. Some were about one-half this size, but not a few involved the entire breast. A little less than 50 per cent of the cases gave a duration in terms of years rather than months, and of this group the duration of 3 or more years was not uncommon. There is a wide age distribution in this group, practically equal numbers occurring in each decade between 30 and 70 years. The occurrence of a sanguineous discharge from the nipple, a location near the center of the breast, and the microscopic appearance justify the conclusion that many of these cases of papillary cancer are late manifestations in a pre-existing benign papilloma.

The tumor in the gross is hemorrhagic, necrotic, or cystic. The cut surface is friable and stringy. The tumor masses are well circumscribed at the periphery, often with a necrotic or cystic center.

Under the microscope the characteristic feature is the persistence of the fibrous stalk supporting loops or folds of glandular cells of varying shapes and sizes. The predominant epithelial cell is malignant in character with a large vesicular nucleus and a moderate amount of cytoplasm. Many of the cells, however, are small and oval in appearance, surrounding a small central lumen to form acinar structures.

In some cases multiple benign papillomas are found in the region of malignant growth upon microscopic examination. In 12 cases multiple tumors in one or both breasts were found in the clinical examination. Microscopically a benign papillary structure is sometimes seen with malignant change at one margin and in 6 cases mucoid degeneration was found in the malignant papilloma. In 12 cases both breasts ultimately were involved.

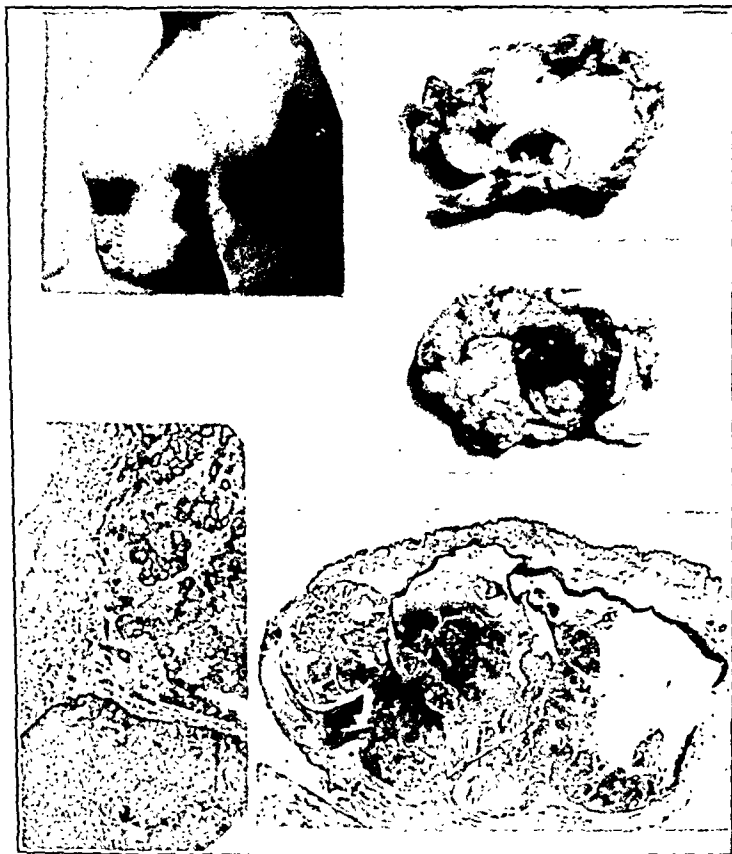


Fig. 12.—Photographs of the patient and the gross specimen and photomicrographs of papillary adenocarcinoma. These tumors are usually sharply circumscribed as shown in the illustrations.

Papillary adenocarcinoma may be cured by radical operation even in advanced cases. Among the five-year survivals, tumors of 5 cm. or larger are nearly as common as those of small size. In 8 cases surviving the five-year period, the tumor was 10 cm. or over in size. In 1 patient who was 69 years of age at the time of examination, a tumor of 14 cm. of 3 years' duration was found. There was a local recurrence 4 years after the radical operation, which was treated by excision, and the patient died of other causes 17 years after the primary operation. A patient with a tumor of similar size died of cancer 17 years after a radical

operation in which the dissection was carried out above the clavicle because of metastases to the glands of the neck. In other cases in which the patient died of the disease, late local recurrence is a striking feature. The recurrence in some instances appeared from 5 to 16 years after the radical amputation. Because of the large size of the tumor, there is a tendency to sacrifice only the skin overlying the mass with very little additional margin. This accounts for the high percentage of local re-

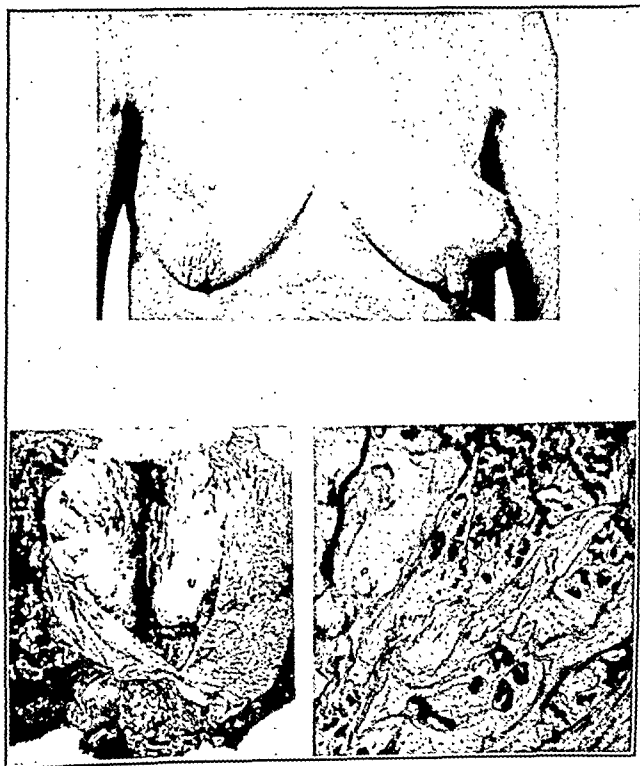


FIG. 13.—Photograph of the patient, gross specimen, and photomicrograph from a case of gelatinous carcinoma. In the photograph of the patient note the enlargement and protrusion of the nipple on the affected side.

currences observed in these cases. Despite the size of the growth and the local recurrences, 60 per cent of the cases survived the five-year period.

#### GELATINOUS, COLLOID, OR MUCOID CANCER

Three per cent of breast carcinoma shows a gelatinous or mucoid intercellular substance in the gross and under the microscope (Fig. 13). The gelatinous character of the tumor has been variously ascribed to degeneration of connective tissue stroma or a secretory product of the epithelial cells. Lang was the first to emphasize the slow growth and relatively benign course of these tumors. Lee, Hauser, and Pack studied

30 cases of mucoid cancer and found the five-year survivals to be 57 per cent as compared to 41 per cent in a control group.

Like papillary carcinoma, mucoid cancer is a slowly growing and low grade form in which arrestment of the disease may be achieved by surgery in advanced cases. Gelatinous carcinoma also resembles papillary cancer in its tendency to occur beneath the nipple (15 out of 75 cases) and to be accompanied by a sanguineous discharge (10 cases). Other similar features are a duration of symptoms of years rather than months, an even age distribution in the decades between 30 and 70 years, an encapsulated and circumscribed character in the gross, which often leads to the clinical impression of a benign lesion, and an association under the microscope with benign intracystic papilloma.

The outstanding clinical features of mucoid mammary cancer are the relatively small size of the tumor in comparison with the long duration of symptoms, the peculiar fluctuant or "swishy" consistency of the tumor suggesting a ruptured cyst, the occurrence of bulging of the nipple rather than retraction when the tumor is in the nipple zone, and the freely movable character of the growth. The average size of tumor in this series was 4.5 cm. and approximately 50 per cent had a diameter of 3 cm. or less. Nearly one-half of the cases had a duration in terms of years rather than months. Nine patients were aware of the tumor for 6 years or longer; 1 had noted the tumor for 48 years, dying with metastases 5 years after operation. A patient who had noted the tumor in the breast 24 years before operation was living and well 15 years after the treatment, and another who had a tumor 8 years died 6 years after a radical mastectomy.

Because of the gelatinous and fluidlike consistency of the tumor and the absence of fixation, the initial clinical interpretation was that of a benign cyst in 11 cases. The occurrence of multiple nodules led to an interpretation of a benign tumor in other instances. Four cases were first diagnosed fibroadenoma; and two, papilloma. In all, 19 cases were initially treated by excision. With few exceptions this was followed by the complete operation within a few days. The differentiation from benign cysts should not be difficult since these cancers are near the skin surface, are less tense and rounded on palpation, and are often accompanied by discoloration of the overlying skin with atrophy of the intervening fat.

The appearance of gelatinous cancer in the gross is characteristic. Gray translucent lobules resembling tapioca or semifluid mucoid material which flows from the tumor on section are diagnostic. Under the microscope, acini or strands of small epithelial cells are dispersed in large amounts of light staining mucoid substance. The microscopic studies indicate that gelatinous cancer is the result of secretory changes in a slowly growing form of adenocarcinoma. In 8 cases in the present series the origin of cancer could be traced to pre-existing benign papilloma. In 1 patient an excision for benign intracystic papilloma

operation in which the dissection was carried out above the clavicle because of metastases to the glands of the neck. In other cases in which the patient died of the disease, late local recurrence is a striking feature. The recurrence in some instances appeared from 5 to 16 years after the radical amputation. Because of the large size of the tumor, there is a tendency to sacrifice only the skin overlying the mass with very little additional margin. This accounts for the high percentage of local re-

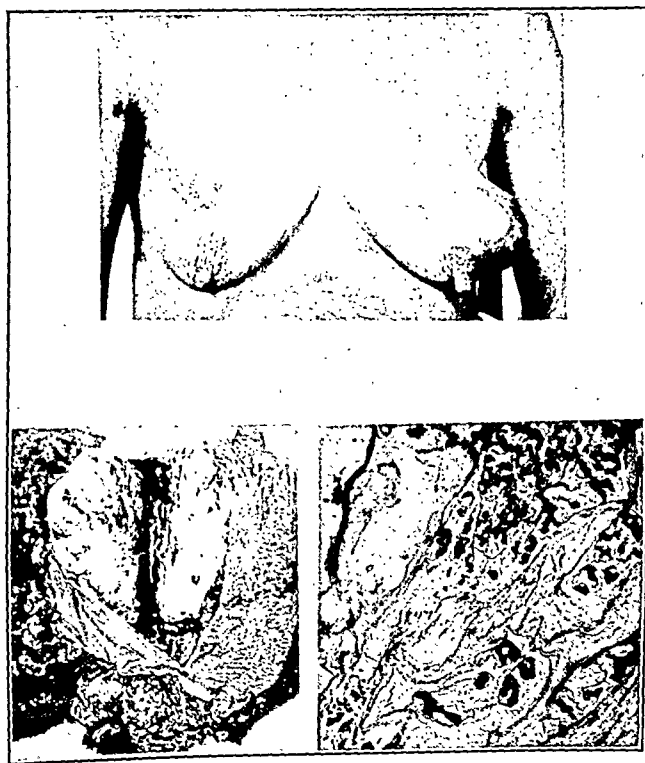


Fig. 13.—Photograph of the patient, gross specimen, and photomicrograph from a case of gelatinous carcinoma. In the photograph of the patient note the enlargement and protrusion of the nipple on the affected side.

currences observed in these cases. Despite the size of the growth and the local recurrences, 60 per cent of the cases survived the five-year period.

#### GELATINOUS, COLLOID, OR MUCOID CANCER

Three per cent of breast carcinoma shows a gelatinous or mucoid intercellular substance in the gross and under the microscope (Fig. 13). The gelatinous character of the tumor has been variously ascribed to degeneration of connective tissue stroma or a secretory product of the epithelial cells. Lang was the first to emphasize the slow growth and relatively benign course of these tumors. Lee, Hauser, and Pack studied

larger ducts and for a long time may remain confined by the normal boundaries of the duct tree. This rare form of mammary cancer which may be associated with adenosis has been termed by Bloodgood comedo cancer. The term comedo is applied to such a tumor because, when it is cut, plugs of tumor cells may be expressed from the ducts similar to the plugs or comedones expressed from an ordinary blackhead on pressure. (Fig. 14.)

There were 136 cases of comedo carcinoma in the present series. In one group, the so-called pure comedo cancer of Bloodgood, the tumor cells at the time of operation had not infiltrated beyond the basement

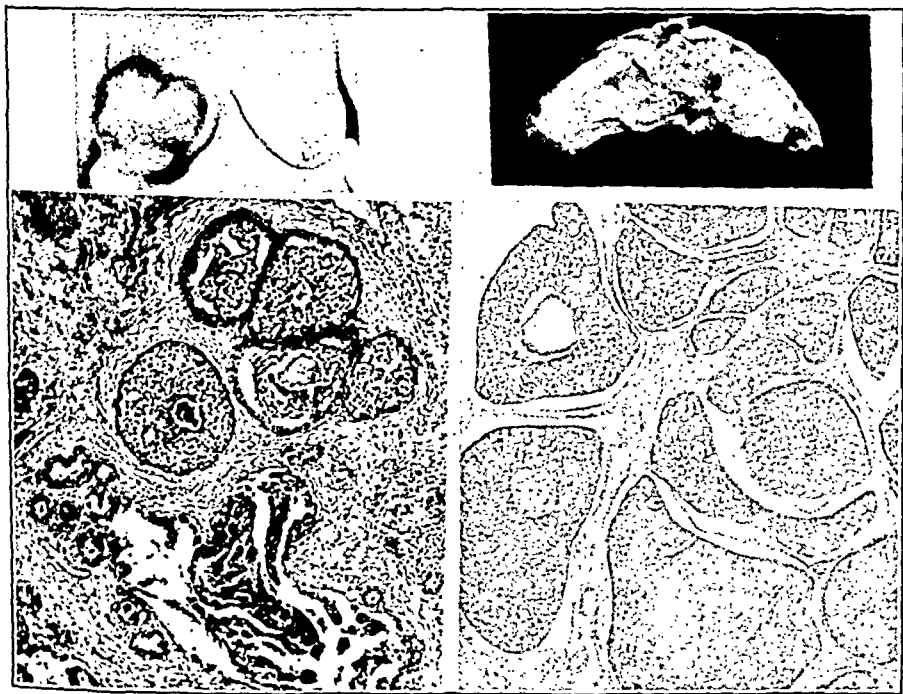


Fig. 14.—Photographs of the patient, the gross specimen, and photomicrograph illustrating the features of comedo carcinoma. The small plugs of tumor tissue can be seen in the gross. The high powered photomicrograph shows the presence of papillary hyperplasia or adenosis in the breast tissue adjacent to the tubules which are infiltrated by cancer.

membrane of the ducts. In the other group of cases, infiltrating comedo carcinoma, the tumor tissue at the time of operation was largely confined within the preformed ducts, but in addition cancer cells infiltrated beyond and invaded fat and fibrous tissue. This group of 135 cancers, which comprises 5 per cent of all forms of mammary cancer, is the only form of malignancy in the present series which showed a tendency to occur in the breast which was the seat of adenosis. Approximately one-third of the cases showed such changes. This form of cancer, moreover, is the most favorable form from the standpoint of treatment and shows 67 per cent of five-year cures.



had been performed 23 years previously and the recurrent tumor at the same site showed, in addition to the characteristic mucoid change, the persistence of a papillary structure. In the majority of cases a papillary structure could not be found and the more solid epithelial portions of the growth suggested a slowly growing adenocarcinoma.

The results of treatment of mucoid cancer are similar to those of papillary cancer in that radical mastectomy accomplishes approximately 60 per cent of five-year cures. In the present series there are 33 cases surviving the five-year period; 27 are known to be dead and 20 are untraced. On the basis of five-year follow-ups (omitting 2 recent deaths), there are 58 per cent of five-year cures. While radical mastectomy is unquestionably the treatment of choice in these cases, 1 patient is reported well 14 years after simple mastectomy and another is living 15 years after excision of a recurrent tumor and 7 years after the local removal of an axillary lymph node which showed metastasis on microscopic examination. In 2 additional cases where excision only was performed, 1 is still living 4 years later, and another died of metastases at the end of 4 years. Two other cases were treated by simple mastectomy. One died two years later and 1 has not been traced. In the cases where simple excision preceded the complete operation, the local removal apparently did not interfere with the percentage of cures established by radical operation.

Although slightly less than 60 per cent survived the complete operation more than five years, there are many cases in this group of survivors that ultimately die of the disease. One patient died with mediastinal metastasis and extension to the neck 35 years after the complete operation and another patient who had the tumor 20 years before the complete operation died of metastasis 6 years after. The fluidlike consistency of the tumor predisposes to transplantation and local recurrence and ultimately to metastases.

#### COMEDO CARCINOMA

The germinal epithelium of the terminal tubules retains the power of growth throughout sexual maturity and is capable of forming additional mammary tubules as well as acini in response to hormonal stimuli during the menstrual cycle or pregnancy. Abnormal hormonal stimuli may result in hyperplasia of these elements, producing minute papillomas and benign adenomas characteristic of the proliferative form of chronic cystic mastitis, or adenosis. Malignant proliferation in these terminal tubules is common after menopause and gives rise to the most prevalent form of mammary cancer, infiltrating scirrhous carcinoma. Our studies have failed to reveal any etiologic connection between the hyperplasia of these germinal buds in adenosis and the malignant proliferation observed in scirrhous carcinoma.

A low grade form of malignancy, however, may arise in the epithelium of the small tubules or from the basal cells beneath the lining of the

patients have remained well more than 20 years, and a fourth patient has remained well for 36 years. The duct carcinoma composed of transitional epithelium related to Paget's disease of the nipple does not afford as favorable a prognosis.

Of 35 patients traced, 1 died of metastases after 5 years, and 3 others died of metastases after 4, 3, and 2 years, respectively. The remainder were well after 5 years (85 per cent five-year cures), but 1 of these died after 6 years, a cancer of the opposite breast having developed.

There were 8 cases of comedo carcinoma in which the initial treatment consisted of local excision. In 6 of these the growth recurred locally—in 1 to 4 years. In these cases radical operation was performed later, and metastases to the axillary nodes were found at the second operation. In the 2 additional cases treated by local excision, 1 of the patients, the wife of a physician, has remained well for 11 years, no other operative intervention having been necessary. A second patient is now well, showing no evidence of recurrence after  $3\frac{1}{2}$  years. One patient was treated with irradiation followed by amputation of the breast without axillary dissection. This operation was performed in May, 1934, and the last report, made at the time of writing, stated that the patient was dying of metastases to the bone and to the skin over the wall of the chest.

*Infiltrating Comedo Carcinoma.*—The pure form of comedo carcinoma just discussed grows slowly and remains confined to the ducts over a period of years and metastasizes very late to the axillary nodes. In the group about to be described, there were 84 cases of infiltrating comedo carcinoma which resembled histologically those previously described but which showed, in addition, cancer cells infiltrating beyond the basement membrane of the ducts and invading fat and fibrous tissue. That this group represents a more rapidly growing form of comedo carcinoma rather than late cases of the pure form is indicated by the age distribution which parallels that of pure comedo cancer, by the shorter duration of symptoms, and by the comparatively small size of the tumor. The average age of infiltrating comedo carcinoma was 45 years compared to an average age of 46.7 years in the noninfiltrating or circumscribed form. The average duration of symptoms in the 28 cases of infiltrating comedo cancer which had noted a tumor for more than a year was  $3\frac{1}{2}$  years and the average duration for 48 cases who had noted a tumor for less than a year was 3.6 months. The average size for all the tumors in the group was 4.8 cm.

The clinical characteristics of these tumors resemble those of the non-infiltrating form of comedo cancer rather than scirrhus cancer in that they are frequently freely movable and are often associated with the larger ducts near the nipple. In this group there were 6 patients treated by local excision in the first instance. One of the recent cases had no further operation. Three had the complete operation within a month following local excision and 2 of these died within a year, the third not being traced. In the 2 remaining cases the excision preceded the com-

The cases of "pure" comedo carcinoma in the 52 patients observed in this series present either of two characteristic clinical pictures. In one, a slowly growing tumor involved the greater part of the affected breast and an isolated tumor could not be palpated in the enlargement. Despite the size of the growth, there were frequently no palpable lymph nodes. In the second, clinical type, the tumor was small, measuring from 1 to 3 cm. in diameter. One or more of such freely movable nodules were palpated just beneath the skin. The age of the patients with comedo carcinoma averages 46.7 years. In about 25 per cent the tumor was of over 2 years' duration, and in 6 it had been noted for 5 years or more. The location of the comedo carcinoma suggests an origin in or near larger ducts. It often develops near the nipple at the margin of the areola, in many cases just above and to the outside of the nipple. Symptoms referable to the nipple are common. A watery milky or yellowish discharge is noted not infrequently. Retraction or fixation of the nipple occurs often, and occasionally the patient complains of burning and itching of the nipple, a symptom more common in Paget's disease. In a few cases a serosanguinous discharge from the nipple was noted.

The tumor is usually located near the skin, and atrophy of the overlying fat and dimpling occur. Redness of the skin is sometimes noted. The tumor remains movable. Even when the growth is larger than 6 cm. in diameter, there will be no fixation to the wall of the chest.

When the tumor is sectioned, characteristic plugs of tumor tissue can be expressed from the larger ducts. The growth is usually infiltrating.

Comedo carcinoma arises from small oval cells with dense nuclei and scanty cytoplasm. There are numerous intermediate cell forms which show a differentiation into duct epithelium with an irregular secretory border. These cells, the nuclei of which show no conspicuous malignant features, form a thick lining or wall in the ducts. The larger secretory epithelium surrounds the central lumen of the duct, which contains secretory debris; the smaller basal cells rest on a basement membrane, which sharply demarcates the duct epithelium from the periductal fibrous tissue. All of the duct channels throughout one or more quadrants of the breast may show this characteristic hyperplasia of the lining epithelium. The tumor cells not only line pre-existing ducts but form new secretory channels, so that small secondary openings appear in the cross sections of the lining epithelium of the larger ducts. The tumor grows slowly and metastasizes late, if at all, to axillary lymph nodes. In cases in which metastases occur, the epithelium in the lymph nodes shows the characteristic thick-walled ducts lined by secretory epithelium with numerous transitions toward basal cells.

Of all the forms of carcinoma of the breast, comedo carcinoma offers the most favorable prognosis. There are 85 per cent of five-year cures in this group of cases. The majority of the patients living more than 5 years after operation have remained well for 10 years or more. Three

selected for special study on the basis of their microscopic appearance. There are two embryonic components from which the breast develops. The more primitive, the milk line, is composed of several layers of thickened epidermis, appearing in the embryo of mammals as bilateral bands connecting the sites of the future nipples. The second embryonic component, mammary bud, appears beneath the milk line. This is a small mound of undifferentiated epithelium derived from the basal cell layers of the epidermis.

In subsequent development the system of primary ducts is formed by the extension of the process of differentiation beginning in the milk line. In the embryo these large milk channels are formed by the hypermaturation of squamous cells which are identical with those found in the epidermis. Ultimately the epidermoid lining of the large mammary ducts is replaced by mammary duct epithelium. However, the persistence of epidermoid cells in the nipple and in the mouths of the larger ducts accounts for the appearance of epidermoid or Paget's cancer in these structures in later life. A persistence or reappearance of the primitive epidermoid lining in the larger mammary ducts some distance from the nipple accounts for a form of duct cancer resembling Paget's disease of the nipple and for epidermoid carcinoma or cancer cysts which may occur deep in the breast tissue.

*Paget's Disease of the Nipple.*—Paget's cancer is characterized by invasion of the epidermis of the nipple or areola and (usually) the mouths of the larger ducts by malignant cells resembling those seen in transitional cell cancer of the skin or mucous membranes. The malignant cells differ somewhat from the usual epidermoid carcinoma and for this reason have become known as Paget cells. (Fig. 15.) The clinical histories are of two types; one in which nipple symptoms precede a tumor in the breast and the other in which a lump in the breast precedes symptoms referable to the nipple.

Regardless of the mode of onset, all the cases of Paget's cancer included in the present study ultimately involved the nipple. The evidence in the present study indicates that cancer of the Paget type begins either in the larger duct beneath the nipple or in the basal cell layers of the epidermis of the nipple itself, in cells predestined to form mammary ducts. That the tumor may begin in the basal cells of the nipple is indicated first by two benign cases in which keratosis of the nipple only was found, at the time of the first examination, and which returned after an interval of a year or more with ulceration of the nipple showing cancerous changes on excision. Second, a series of 19 cases where malignant Paget cells were found in the nipple, in which either the simple mastectomy or radical mastectomy was performed, and subsequent examination of the amputated breast failed to reveal any evidence of the disease outside of the nipple. Third, a

plete operation by more than 1 year. Both, however, have remained well for 14 years following the complete operation.

At the time of writing, 27 cases have not been traced for a period sufficient to learn the results of treatment and 55 have been followed. Twenty-seven of the followed cases are known to be dead, and 28 have survived the five-year period. All the cured cases except the 2 just mentioned were treated by radical surgery. None of the cured cases received preoperative irradiation. There are 51 per cent of five-year survivals.

1

#### PAGET'S DISEASE OF THE NIPPLE AND DUCT AND PAGETOID CANCER OF THE BREAST

Since Paget's clinical description in 1874 of cancer of the female nipple and Butlin's microscopic study of the disease in 1876, cancer of the breast characterized by large cells resembling squamous epithelium has been recognized as a separate form. The exact definition or limit of the disease, however, has been much disputed. Clinically there has been a tendency to classify as Paget's disease any lesion of the breast producing destruction of the nipple. However, cancer characterized by large epidermoid-like cells of the Paget type may occur in the breast without involving the nipple. A definite group of carcinoma of the ducts resembling Paget's cancer of the nipple under the microscope may remain confined to the ducts or invade the substance of the mammary gland and not the nipple. Another group of cases of so-called cancer cysts contain epithelium resembling the Paget type but arise within the substance of the gland.

In the 2,300 cases of cancer of the breast in the present series there were 62 cases which had been routinely classified as Paget's cancer. These were characterized by lesions of the nipple and by the presence of typical Paget cells which involved the nipple and with few exceptions the mouths of the adjoining ducts. In 40 of these cases a cancerous mass was also found in the mammary tissue at some distance from the nipple. There was a second group of 25 cases of duct carcinoma in which the tumor was characterized by large "Pagetoid cells," originating in and for the most part confined to the larger ducts. Seven of these were accompanied by a discharge from the nipple but none produced ulceration or histologic invasion of that organ. There was a third group of cancers histologically resembling Paget's disease of the nipple or Pagetoid duct cancer. This group of 74 carcinomas of the breast showed little or no tendency to involve the larger ducts or to invade the nipple. They gave rise to distinct mammary tumors which were usually characterized in the gross as cancer cysts, the enclosed cavity containing blood or necrotic tissue.

These three groups of carcinoma totaling 161 cases apparently arise from a more primitive form of transitional epithelium and have been

In some instances there was gradual retraction and disappearance of the nipple, the nipple being replaced by an ulcer. In a few instances the area of ulceration was in the areola and not in the nipple itself.

Nearly 50 per cent of the patients were 50 years of age or over, and the majority were past the menopause. In 10 cases the patients were 65 years or over. The usual duration of symptoms was between 1 and 3 years. In 12 cases the duration was 5 years or over. Distinct papillary or warty projections of the epidermis covered by roughened but intact mucous membrane apparently bear no relationship to cancer.

The distinction between benign and malignant lesions of the nipple cannot be made clinically in cases of keratosis and ulceration in which a mass palpating like cancer is not found in the underlying breast. During the corresponding period in which 62 cases of Paget's cancer were observed, 82 benign lesions of the nipple were recorded. In 40 of these cases of keratosis, a few of which were complicated by ulceration and red granular nipple, the benign nature of the lesion was established by healing and disappearance of the lesion upon applications of petrolatum following cleansing of the nipple with soap and water over a period of three to four weeks. In the other 42 cases healing did not occur when such cleansing and protective measures were instituted. These cases, with 5 exceptions, were treated by excision, and microscopic study failed to reveal evidence of malignancy. In the 5 exceptional cases observed prior to 1920, simple mastectomy or the radical operation was performed because the lesions were considered clinically malignant although pathologic study failed to reveal evidence of carcinoma.

A pathologic study of the breast removed in cases of Paget's cancer of the nipple shows, in addition to the keratotic or ulcerated lesion of the nipple, dilatation of the larger ducts in the nipple zone. Occasionally these ducts are filled with blood or inspissated secretion. In other cases the dilated ducts are distended with cancer cells. In 1 case a small encapsulated lesion measuring 5 mm. was found just beneath the nipple. This was microscopically composed of cancer cells. The occurrence of a definite infiltrating mass in the mammary tissue outside the nipple zone occurred in slightly over 60 per cent of the cases. With few exceptions these cases also showed metastasis to the axillary lymph nodes. In 1 case the nipple and axillary nodes were involved and no cancer could be demonstrated in the mammary tissue.

The cases classified as Paget's cancer in the present series in every instance contained large cells with deep staining or vesicular nuclei and a large amount of pale staining cytoplasm in the epidermis of the nipple. Mitotic figures are frequent. In 2 cases the Paget cells were found only in the epidermis of the nipple or areola and no malignant cells could be found in the adjoining ducts or underlying mammary tissue. In the remaining cases the larger ducts were involved and the

small group of cases in which Paget cells were found in the nipple and cures were established by local excision.

That Paget's cancer may begin in a duct beneath the nipple is indicated by a group of duct cancers, with Pagetoid cells (to be described subsequently) which do not involve the nipple and by a few cases of this type which showed involvement of the nipple late in the course

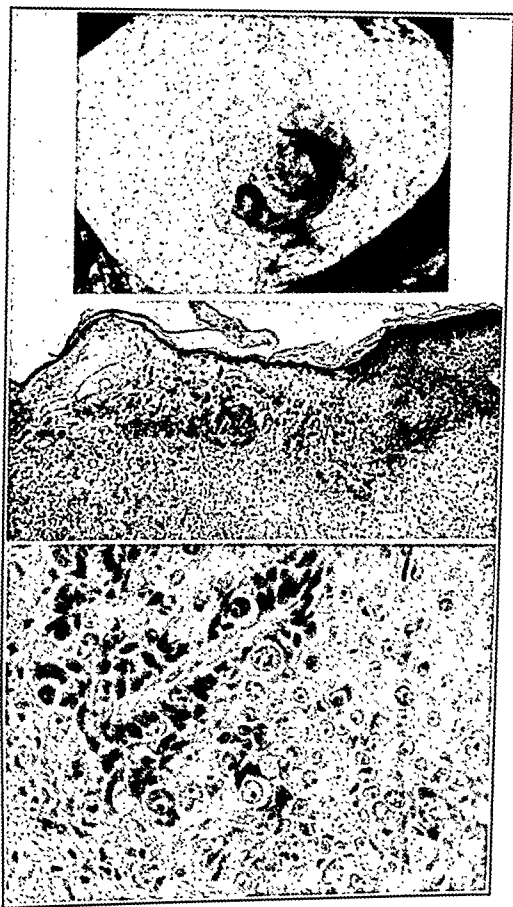


FIG. 15.—Photographs and photomicrographs of involvement of the nipple by Paget's cancer.

of the disease. This is also suggested by those patients who have noted a mass in the breast for months or years before noting changes in the nipple.

The symptoms in Paget's disease relate to the nipple whether or not a mass is found in the underlying breast. Itching, burning, pain, or soreness is noticed first but in some instances discharge, crust, or scabs were first observed. Fissure or ulceration usually developed in the cases which microscopically proved to be malignant, although in exceptional instances the nipple was red and large and finely granular.

cancer tissue is demonstrated in the mammary gland, the chances of the patient surviving the five-year period are less than 10 per cent (8 per cent in this series).

*Paget's Cancer of the Ducts.*—In the present series there were 23 cases of carcinoma which involved the larger ducts of the breast and which, on the basis of histology, could be related to the group of Paget's cancer just described. The tumor cells lined the ducts in broad sheets or multiple small papillary-like masses. The cells are

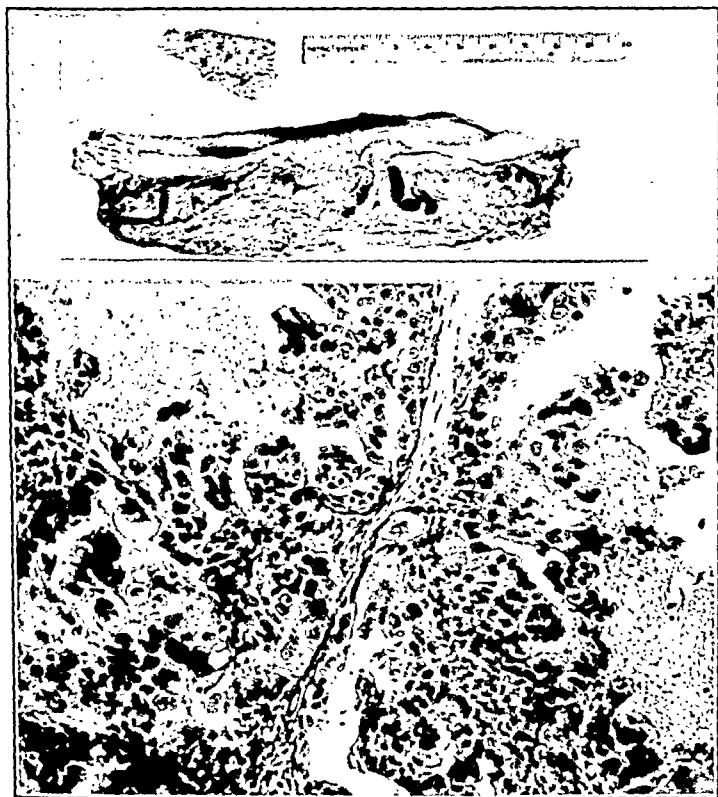


FIG. 16.—Gross specimen and photomicrograph of a case of duct cancer of the Paget type. The nipple was not involved in this case.

large and have an abundant cytoplasm with immense dense or vesicular nuclei with numerous mitoses. (Fig. 16.) Multinucleated giant tumor cells are common. The involvement of the larger ducts is similar to that found in Paget's disease in all respects except the nipple is not involved. This group of cases apparently represents the earliest stage of Paget's cancer which begins in the larger ducts within the breast proper rather than in the nipple. One-half of the cases gave a duration of symptoms of two months or less, a finding in keeping with this interpretation. None of the tumors exceeded 4 cm. in diameter. Fifteen of the 25 patients in this series, all of whom were treated by



cells in the nipple were infiltrated beyond the basement membrane. The ducts were lined by many layers of large malignant epithelium with necrotic debris or secretion in the enclosed lumen. Where the ducts only were involved in addition to the nipple, the growth in the ducts showed a histologic picture under low power suggesting the type of cancer loosely referred to as comedo or duct cancer. When the breast tissue was invaded, the microscopic appearance is that of Grade IV scirrhous carcinoma, but under high power the cells are larger, more irregular in shape, contain numerous mitotic figures and tumor giant cells, and in general resemble epidermoid carcinoma although no keratinization is found.

In the present series 22 cases of Paget's cancer clinically and on pathologic examination showed no mass within the breast proper. Three of these cases were treated by simple excision of the nipple and underlying ducts and fat. Three had simple amputations of the breast and the remainder were treated by radical mastectomy. One of the cases treated by local excision died of cancer 3 years later and 1 treated by simple mastectomy died of recurrent cancer 1 year later. The 2 remaining cases treated by excision were well 7 and 10 years later. In 1 both nipples were involved. In the 2 remaining cases receiving simple amputation, 1 died of metastasis 5½ years later and the other of old age after 8 years. In those cases treated by radical mastectomy in this group where the cancer was confined to the nipple and adjoining ducts, none so far traced has failed to survive the five-year period. Six have not been traced and 14 are cured.

There were 40 cases of Paget's cancer in which in addition to the nipple lesion there was a mass in the underlying breast, usually palpated before operation. All of these cases were treated by radical mastectomy. Twenty-three died of the disease within less than 5 years, the majority within a period of 1 or 2 years. Fifteen have not been traced. Two cases survived the five-year period. One of these died after 6 years, the other is living and well 10 years later.

Irradiation has failed to eradicate the disease as shown by cases ultimately treated by mastectomy, and Cohn has reported instances where irradiation was followed by healing of the lesion of the nipple but continued growth and spread of the disease occurred in the breast beneath. Keratosis, fissures, ulcerations, and red granular changes in the nipple should be treated by excision of the nipple zone with a margin of skin and a core of underlying ducts and fatty tissue, in those cases where the lesion fails to heal within three or four weeks after cleansing and protective measures. The excised tissue should be subjected to microscopic study and, if cancer is found, radical mastectomy is indicated. In those cases where cancer is not found in the underlying breast tissue, cures will be effected by this treatment. Where

cancer tissue is demonstrated in the mammary gland, the chances of the patient surviving the five-year period are less than 10 per cent (8 per cent in this series).

*Paget's Cancer of the Ducts.*—In the present series there were 23 cases of carcinoma which involved the larger ducts of the breast and which, on the basis of histology, could be related to the group of Paget's cancer just described. The tumor cells lined the ducts in broad sheets or multiple small papillary-like masses. The cells are

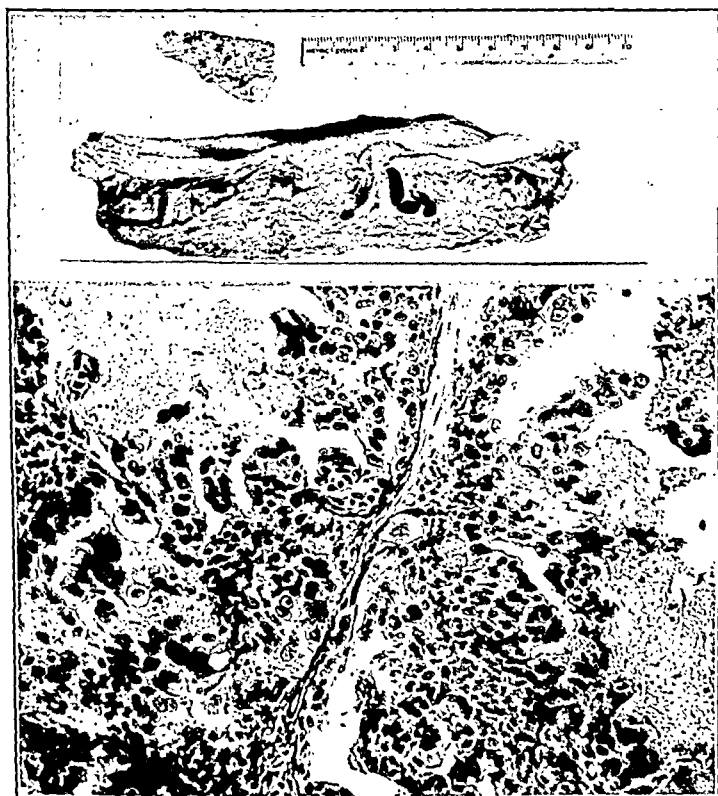


Fig. 16.—Gross specimen and photomicrograph of a case of duct cancer of the Paget type. The nipple was not involved in this case.

large and have an abundant cytoplasm with immense dense or vesicular nuclei with numerous mitoses. (Fig. 16.) Multinucleated giant tumor cells are common. The involvement of the larger ducts is similar to that found in Paget's disease in all respects except the nipple is not involved. This group of cases apparently represents the earliest stage of Paget's cancer which begins in the larger ducts within the breast proper rather than in the nipple. One-half of the cases gave a duration of symptoms of two months or less, a finding in keeping with this interpretation. None of the tumors exceeded 4 cm. in diameter. Fifteen of the 25 patients in this series, all of whom were treated by

radical operation, have been traced. Two were well after 4 years. Of the remaining 13, 7 died of metastases and 6 were well over 5 years.

*Epidermoid or Pagetoid Cancer of the Breast.*—In the present series there were 74 cases of cancer which resembled histologically the cases of Paget's disease of the nipple and Paget's cancer of the ducts. The age distribution in this group is similar to that for mammary cancer in general. The tumors were most often located in the midzone of the breast. With few exceptions they were embedded deep in mammary

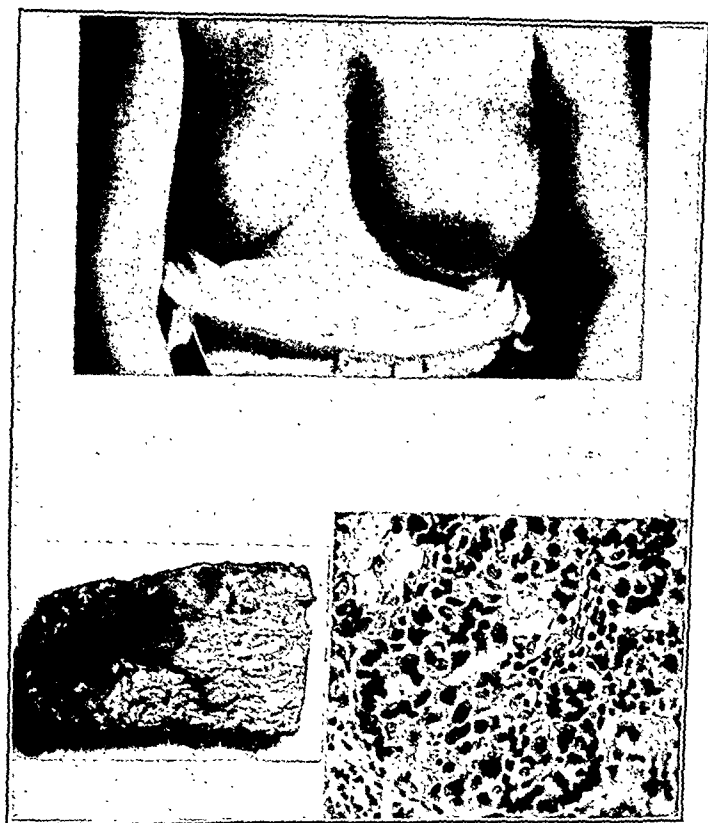


Fig. 17.—Photograph of the patient, gross specimen, and photomicrograph from a case of transitional cell (Pagetoid) carcinoma of the breast. The photomicrograph shows the resemblance of this form of cancer to epidermoid carcinoma.

tissue and one-fifth of the number were located in the lower hemisphere of the breast. The tumors resemble other forms of carcinoma in their tendency to grow rapidly without pain and ultimately to produce discoloration, edema, and ulceration of the overlying skin. The average size of the tumors in the series was 4.8 cm. The mass was usually regular on outline and circumscribed. (Fig. 17.) Most often it was freely movable. In nearly one-sixth of the cases the impression of benign cyst was obtained before operation and several were aspirated and a yellowish or bloody fluid obtained. In 5 cases the mass was

thought to contain multiple cysts, 1 giving the clinical impression of polycystic disease. In 5 cases the disease involved both breasts at intervals of 2 weeks, 1 year, 2 years (2 cases), and 6 years. The majority of the women affected had borne three or more children and an apparently significant number recalled a severe blow at the site where the tumor developed.

The most characteristic features are in the gross and microscopic pathology. In the gross pathology, with few exceptions, the tumor was classed as a cancer cyst. The tumor contained a distinct wall, sometimes uniformly thick and other times thinned at one or more portions. If the wall was relatively smooth and the cavity large, the cyst contained bloody fluid, a finding which rules out the possibility of a benign blue dome cyst. In other cases granular, grumous, necrotic, or pulpy material occupied the cavity. No distinct papillomatous mass was noted, a point which distinguishes them from papillary cancer.

Microscopic examination of the tumor tissue shows large highly malignant tumor cells, growing in sheets or coiled membranes. The nuclei are hyperchromatic, variable in size and shape, and contain frequent mitotic figures and binucleated forms. In 8 cases there was frank squamous cell cancer in the cyst lining. Some were apparently related to benign dermoid cysts and showed keratinization and pearl formation.

All of the 74 cases were treated by radical mastectomy, despite the fact that some were explored for a benign cyst. Twenty-two survived the five-year period and of these only 3 were known to have died ultimately of the disease. Thirty-eight died of the disease, with few exceptions in less than 4 years. The remaining cases were untraced. There are 32 per cent of five-year cures.

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# Review of Recent Meetings

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## REVIEW OF THE THIRTEENTH ANNUAL MEETING OF THE PACIFIC COAST SURGICAL ASSOCIATION, LOS ANGELES, CALIF., FEB. 22-25, 1938

HENRY H. SEARLS, M.D., SAN FRANCISCO, CALIF.

Dr. Wayland A. Morrison, Los Angeles, Calif., in the President's Address, discussed the continued trend toward specialism in medicine, noting that the modern surgeon works hard and dies early. He advised less vocation and more avocation.

Dr. Howard C. Naffziger, San Francisco, Calif.: **Experiences With Injuries of the Intervertebral Disks and Ligamenta Flava.**—In Dr. Naffziger's absence this paper was presented by Dr. Howard W. Fleming, San Francisco, Calif. The essayist described the anatomy of the vertebral column and its fibrous and cartilaginous attachments with special reference to the ligamentum flavum and the intervertebral disks. The close relationship of the ligamentum flavum to the nerve roots was pointed out. Injury to this ligament results in hypertrophy and pressure on the neighboring nerve root. In other instances abnormal pressure on the vertebral column causes herniation of the soft nucleus pulposus through the thin posterior portion of the annulus fibrosus. The projection backward of this herniating fibrous material causes pressure on the cord or the branches of the cauda equina. The typical picture is that of a male in the active period of his life, who has a history of trauma, followed by sciatic pain which is aggravated by coughing or straining. The pain radiates to the outer side of the leg and to the dorsum of the foot. There is an absent or altered Achilles reflex on the affected side. Sensory changes may be noted on the outside of the calf; there is muscular weakness, and pain is present on straight leg raising. X-ray examination of the lower spine, following the administration of lipiodol intrathecally, shows a characteristic filling defect, which is diagnostic. Relief follows laminectomy and removal of the hypertrophied ligamentum flavum or herniated nucleus pulposus. In the discussion, Dr. Harold Hitchcock, Oakland, Calif., suggested spinal fusion following laminectomy in order to prevent weakening of the vertebral column by the operation. Dr. Frederick Reichert, San Francisco, Calif., felt that lipiodol left in the spinal canal might be injurious and suggested air as a substitute. In closing, Dr. Fleming agreed that the laminectomy might weaken the spine sufficiently to cause symptoms in a man who is doing heavy work, and felt that fusion might be necessary in such instances. He had not been impressed by the diagnostic accuracy of x-ray studies after the use of intrathecal air in place of lipiodol.

Dr. Fred R. Fairchild, Woodland, Calif.: **Supplementary Report on the Discussion of Appendicitis Given in 1930.**—Having reported a series of over 500 appendectomies in a first paper presented in 1930, Dr. Fairchild offered for comparison a new group of similar size which had accumulated since that time. He pointed out that, in both series, the mortality was eight times greater in the sec-

ond half of life. There were no deaths in the second series when operation was performed within twenty-four hours of the onset of the attack. In his first series the mortality was 4.4 per cent; in the second, 1.37 per cent. He attributed the improvement to (1) less delay, (2) the use of a gridiron incision, (3) the reduction of the operative procedure to the simplest possible type in patients in the second half of life, and (4) the use of drainage rather than appendectomy in all patients for whom there was doubt in the surgeon's mind as to the safety of appendectomy. The paper was discussed by **Dr. William A. Taylor**, Ellensburg, Wash., who recommended a delay of from eight to fourteen days in all patients whose illness was of more than twenty-four hours' duration. He reported 3 deaths in 557 cases. **Dr. E. C. Moore**, Los Angeles, Calif., suggested the employment of regional or spinal anesthesia.

**Dr. Alson R. Kilgore and Dr. Leroy C. Abbott**, San Francisco, Calif.: **Sarcoma Following Benign Bone Lesions.**—The essayists pointed out the danger of secondary sarcomatous degeneration in some of the benign bone lesions and reported such a development in a case of chondroma. **Dr. E. I. Bartlett**, San Francisco, Calif., suggested the use of x-ray in central chondromas. **Dr. Donald V. Trueblood**, Seattle, Wash., discussed the pathologic phase of the problem and warned that a bizarre pattern in the benign lesion carries the threat of malignant degeneration.

**Dr. John C. Wilson**, Los Angeles, Calif.: **The Circulation of the Upper End of the Femur and Its Relationship to Trauma.**—Dr. Wilson pointed out that no blood vessels are found in the ligamentum teres in early or late life and, therefore, in fracture of the neck of the femur associated with rupture of the ligamentum teres, aseptic necrosis of the head is the common end-result. He felt that fracture of the neck of the femur in children is very serious and leads to grave disability. The immediate results are good, but in from ten to twenty months aseptic necrosis develops. Similar complications are found in late life.

**Dr. E. C. Moore**, Los Angeles, Calif.: **Chronic Cholecystitis with Reference to the Spastic Colon.**—Dr. Moore urged extreme care in the diagnosis of gall-bladder disease without stones. An irritable colon as the source of symptoms must be ruled out by therapeutic test. In the latter condition a definite history of colic or jaundice notably will be absent. X-ray examination, including barium enema and cholecystography, should always be employed. Gall-bladder disease and irritable colon cannot be differentiated by symptoms alone in many cases. The irritable colon, however, is functional and will respond to medical therapy. Dr. Moore emphasized here the importance, as in cases of peptic ulcer, of cooperation between the surgeon and the internist. If there is no history of acute gall-bladder colic or jaundice, he recommended medical treatment for colitis first as a therapeutic test. **Dr. Thomas Joyce**, Portland, Ore., suggested that the relief of gall-bladder disease might help a spastic colon. **Dr. L. R. Chandler**, San Francisco, Calif., noted improvement of gall-bladder function after a spastic colon had been returned to a normal state.

**Dr. Edgar L. Gilcreest**, San Francisco, Calif.: **Lesions of the Shoulder, with Special Reference to Unusual Ruptures of the Muscles of the Shoulder Girdle and Upper Arm.**—In most patients complaining of pain in the shoulder, extra-articular lesions, rather than arthritis, are the source of the trouble. Fraying or rupture of the supraspinatus tendon is not uncommon. Rupture of the biceps and triceps has been encountered frequently.

**Dr. C. G. Toland and Dr. William P. Kroger, Los Angeles, Calif.: Benign Tumors of the Stomach; Report of a Case.**—Myomas comprise the majority of benign gastric tumors. They rarely cause symptoms unless complications develop—such as ulceration, hemorrhage, pressure, or, rarely, malignant degeneration. If intraluminal, benign tumors may obstruct the pylorus; if extraluminal, they may cause symptoms by pressure. The authors reported a case of a large extraluminal myoma, arising by a pedicle from the posterior gastric wall and lying in the lesser sac. A filling defect seen by x-ray was first thought to be caused by carcinoma, but later the roentgenologist diagnosed a benign lesion. Peritoneoscopy identified the tumor as presenting below the greater curvature of the stomach. At operation the pedicle was transected and the tumor removed easily. It weighed 700 gm. The pathologic diagnosis was leiomyoma. The patient recovered. **Dr. Verne C. Hunt, Los Angeles, Calif.,** described two origins of benign tumors—papillomas and adenomas from the epithelial layer, and myomas and fibromas from the connective tissue and muscular layers of the stomach wall. He noted that malignant degeneration is especially common in the case of papillomas.

**Dr. William J. Norris, Los Angeles, Calif.: Intestinal Obstruction in Infancy and Childhood.**—Dr. Norris reported 100 cases (treated by various surgeons in Los Angeles), including cases of intussusception, atresia, stenosis, obstruction from postoperative adhesions, malformed or imperfect anus, volvulus, obstruction from Meckel's diverticulum, intra-abdominal herniation, and stenosis from the ingestion of strong chemicals. Delay was considered the most important factor in mortality. No patient requiring resection recovered. He recommended, therefore, exteriorization for gangrenous loops. Factors which contribute to a reduction in mortality are: (1) early diagnosis, (2) avoidance of complicated procedures, (3) the preoperative treatment of dehydration and the use of measures to obtain decompression, and (4) the use of the least amount of surgery that can be done. **Dr. Otis Lamson, Seattle, Wash.,** emphasized the seriousness of obstruction in infants and reported a case. **Dr. H. Glenn Bell, San Francisco, Calif.,** stressed the importance of adequate preoperative care, the administration of parenteral fluids and blood transfusions, and reported several cases.

**Dr. Paul C. Gunby, Seattle, Wash.: Congenital Pulmonary Cyst; Report of a Case.**—The common error of calling this disease chronic empyema was emphasized and a case was reported of solitary congenital pulmonary cyst, which was finally recognized and cured by excision. **Dr. Frank S. Dolley, Los Angeles, Calif.,** reported several similar cases and discussed the mechanics of their development.

**Dr. Irving Wills and Dr. P. A. Gray, Santa Barbara, Calif.: Diabetic Surgery. II. End-Results.**—These authors emphasized the fact that the diabetic patient, because of his metabolic defect, is more prone to infection, acidosis, and peripheral circulatory collapse than the normal person. Because of unfortunate experiences with the less radical procedure, they recommended high amputation, under spinal anesthesia, in cases of diabetic gangrene of the foot or leg. Postoperatively, the blood sugar determination should be made every four hours and sufficient insulin administered to maintain the blood sugar at from 100 to 150 mg. per cent. They recommended radical removal of thyroid tissue in toxic goiter and noted that such patients often require less insulin after operation. In emergencies, they operate at once unless the patient is in ketosis. Throughout the paper, they stressed the importance of cooperation with a good internist and laboratory technician. With such cooperation, any operation can be undertaken safely on the diabetic patient. **Dr. P. A. Gray, Santa Barbara, Calif.,** emphasized the gravity of peripheral circulatory collapse and suggested the use of

a large amount of fluid to prevent or overcome it. **Dr. Verne C. Hunt**, Los Angeles, Calif., pointed out that anesthesia and operation temporarily upset the chemical balance and cause sudden wide variations in the blood chemistry.

**Dr. Charles Fox**, San Diego, Calif.: **The Treatment of Deep Infections of the Neck.**—Dr. Fox discussed the anatomy of the fascial spaces and pointed out that pus under the deep fascia cannot be demonstrated clinically. He felt that abscesses forming in this region do not give the impression of fluctuation because of the overlying fascia. He urged early incision and drainage and decried the delay in waiting for pointing. The deep fascia prevents the pus from coming to the surface. **Dr. E. I. Bartlett**, San Francisco, Calif., believed that infected teeth are most often the source of abscess formation under the deep fascia.

**Dr. Philip K. Gilman**, San Francisco, Calif.: **Malignant Disease of the Small Bowel.**—Cancer of the small bowel is twice as frequent in the male as in the female. It is rare, as compared to cancer in the colon. It is usually annular and constricting, and obstructive symptoms often are the first indication of the disease. Progressive pain after meals, colicky in character, occurring in the epigastrium above the umbilicus, associated with constipation and vomiting, suggests the development of chronic obstruction. A mobile mass may be felt; blood is usually present in the stool. The diagnosis usually can be made by x-ray examination. Glandular metastases may occur early. Treatment consists of resection, with removal of regional lymph nodes, but the prognosis is very grave. The essayist suggested a method of excision with extra-abdominal clamping of the transected ends and secondary intraperitoneal anastomosis after 24 hours. He reported three cases. **Dr. Thomas Joyce**, Portland, Ore., emphasized that pain is a prominent symptom in malignancy of the small bowel, and that occult blood is a frequent finding.

**Dr. W. D. Kirkpatrick**, Bellingham, Wash.: **Mesenteric Lymphadenitis in Relation to Intestinal Obstruction.**—Mesenteric lymphadenitis is most often found between the ages of 15 and 30 years; both tuberculous and nontuberculous types are noted, and either may be calcified. He reported a case of obstruction in an elderly patient, caused by a large, calcified mesenteric lymph node. **Dr. William J. Norris**, Los Angeles, Calif., noted that either caseation or calcification in mesenteric tuberculous adenitis tended to cause the formation of adhesions.

**Dr. Samuel Robinson**, Santa Barbara, Calif.: **A Case of Rupture of the Small Bowel without External Trauma or Pathology.**—The author reported a case of spontaneous rupture of the bowel, probably caused by extreme intra-abdominal pressure associated with athletic effort, forcing a portion of the bowel wall into a small inguinal hernial sac and rupturing it. He suggested that the mechanism was similar to that of an inner tube, bursting through a defect in an automobile tire. His patient had an extremely stormy postoperative course, developing several fecal fistulas, which were treated by means of intra- and extraluminal rubber disks sewed together, which temporarily closed the openings. The patient was finally sufficiently improved to permit reoperation and resection of the fistulous loops, and made an excellent recovery. **Dr. C. G. Toland**, of Los Angeles, Calif., having been in consultation on this patient, described the infinite care which the patient received in the effort to improve his condition to the point at which a secondary operation could be performed. **Dr. Edmund Butler**, San Francisco, Calif., reported a similar case in which intestinal contents were found in the sac of an inguinal hernia.



# REPORT ON THE MEETINGS OF THE AMERICAN SOCIETY FOR PHARMACOLOGY AND EXPERIMENTAL THERA- PEUTICS, BALTIMORE, MD., MARCH 30—APRIL 2, 1938

RAYMOND N. BIETER, M.D., ST. PAUL, MINN.

(From the Department of Pharmacology, the University of Minnesota Medical School)

THE pharmacology of sulfanilamide continues to be a question of major importance. An afternoon discussion meeting on this subject was conducted under the direction of Dr. E. K. Marshall, Jr., and Dr. Perrin H. Long, Baltimore, Md. A considerable number of pharmacologists and other interested investigators participated. The first question considered was that of the therapeutic effects obtained in experimental infections in animals. It was agreed that even this question presented many difficulties, such as variations in the virulence of the organisms and the resistance of the host and how and when to administer the drug. An example of this latter difficulty is described. One large dose of sulfanilamide each 24 hours administered to mice infected with meningococci was no more curative than a mediocre serum. If the same total amount of the drug was given in two or more divided doses each 24 hours, the curative effects became marked.

The second question considered was that of therapeutic effects in patients. The most striking results have been obtained in the treatment of meningococcus infections. The next most satisfactory results have occurred in infections due to the beta hemolytic streptococcus. Less remarkable results, to date, have been observed in infections due to either the typhoid or the Welch bacillus, and in urinary tract infections due to gram-negative bacilli and staphylococci. In the treatment of pneumococcus lobar pneumonia the drug appears to be of no value, although in meningitis due to this same organism occasional good results have been obtained. It was also brought out that the drug shows its most marked therapeutic effect in acute infections of a highly invasive type.

The toxicity of sulfanilamide was the third question discussed. As is commonly known, the acute toxicity is rather low. Four investigators reported the lethal dose for 50 per cent of a series of mice to be from 3.5 to 4 gm. per kilogram of body weight. The chief toxic reactions observed clinically have been: (a) minor cerebral reactions, such as listlessness, dizziness, nausea, etc.; (b) fever and skin rashes; (c) cyanosis; and (d) the most dangerous reactions, namely, acute hemolytic anemia and agranulocytosis. To date, it has been quite difficult to duplicate these reactions in animals. No one has reported any changes in the red or white blood cells in animals, and only occasionally has cyanosis been observed in experimental work. The closest approximation to human toxic reactions was reported by Dr. S. M. Rosenthal, and Dr. H. Bauer, Washington, D. C., from the National Institute of Health. Their derivative, disulfanilamide, produced polyneuritis when used clinically. Returning to experimental conditions, they have found that this drug, and also sulfanilamide itself, commonly produces symptoms of polyneuritis and neuromuscular paralysis when administered daily for a period of a week to ten days to rabbits and chickens. On the other hand, with a sulfoxylate derivative of sulfanilamide, no such symptoms were noted. Several other investigators have also noted symptoms of peripheral neuritis in experimental animals receiving repeated daily doses of sulfanilamide.

The fourth and last question considered was the mechanism of action of sulfanilamide. Studies to date have been concerned largely with the action of the drug against the beta hemolytic streptococcus. Its chief mode of action on this organism is believed to be one of bacteriostasis. A bactericidal action also can be obtained in vitro, but no evidence of this action has so far been noted in vivo. Other factors mentioned were the question of the drug combining with bacterial toxins, phagocytosis, and the possibility of the drug combining with the proteins of the body of the bacteria. It was also the opinion of a number of investigators that the natural resistance of the patient was a factor of considerable importance. In the final analysis, no definite conclusions could be drawn, because even in many patients treated, and to all intents and purposes cured, the beta hemolytic streptococcus persists for at least a number of days thereafter.

A number of interesting papers relating to general anesthesia were reported. Dr. M. H. Seevers, Dr. W. H. Cassels, and Dr. T. J. Becker, Madison, Wis., from the University of Wisconsin have been studying the problem of "ether convulsions" in rats and dogs. They considered the following factors: the anesthetic itself, pyrexia, and CO<sub>2</sub> retention. The anesthetic alone produced muscle twitchings in a single instance. Pyrexia alone produced no symptoms. Concentrations of CO<sub>2</sub> alone, especially above 20 per cent, elicited muscle twitchings more commonly. When these three factors were combined, muscular twitchings and convulsions occurred in more than 60 per cent of the animals. The convulsions, moreover, were frequently followed by death of the animals. Similar results were obtained in rabbits and dogs with the usual anesthetic concentrations of cyclopropane. Where the fundamental causes of these convulsions are unknown, they suspect that one of the chief factors is a lowering of blood pH, which is exaggerated by or associated with fever and rebreathing of CO<sub>2</sub>, for a sufficient intake of oxygen will not prevent the convulsions.

Dr. B. H. Robbins, Dr. J. H. Baxter, Jr., and Dr. O. G. Fitzhugh, Nashville, Tenn., from Vanderbilt University, reported upon a study of the blood concentration of cyclopropane, in dogs, necessary to produce general anesthesia after premedication with morphine, sodium barbital and sodium amytal. The following table obtained from one of their slides illustrates the results they have obtained:

DRUG USED FOR PREMEDICATION AND DOSE IN MG. PER KG.	CYCLOPROPANE IN MG. PER 100 C.C. BLOOD NECESSARY TO PRODUCE			
	A ABOLITION OF ABDOMINAL REFLEXES (MG.)	B ABOLITION OF LID REFLEX (MG.)	C OCCURRENCE OF INTERCOSTAL PARALYSIS (MG.)	D OCCURRENCE OF RESPIRATORY ARREST (MG.)
None	16.8	20.6	25.5	28.0
Morphine, 2 mg.	8.7	15.1	25.0	29.9
Morphine, 5 mg.	6.0	12.4	21.1	28.5
Sodium barbital, 150 mg.	5.6	10.4	18.7	24.1
Sodium amytal, 45 mg.	5.0	6.9	17.0	25.2

It can be seen that the three drugs used for premedication all greatly lower the blood concentration of cyclopropane necessary to produce general anesthesia (second, third, and fourth planes of Stage 3), without greatly lowering the amount necessary for respiratory arrest. This evidence of increased safety is of great practical importance.

Dr. R. M. Waters, Dr. J. H. Bennett, and Dr. M. D. Leigh, Madison, Wis., from the University of Wisconsin, have studied the effect of combining atropine or scopolamine with morphine as a premedication for general anesthesia. Both alkaloids counteract, slightly, the mild depression of therapeutic doses of morphine on respiration. In addition, scopolamine seems to produce a more effective control of the morphine nausea. They believe that the optimum mixture is morphine 25 parts plus scopolamine 1 part (morphine sulfate  $1/4$  gr., and scopolamine hydrobromide  $1/100$  gr.) and that their maximum action is produced about one and one-half hours after hypodermic administration. This means, therefore, that for premedication, the drugs should be given from one to one and one-half hours before the general anesthetic.

## Book Reviews

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**Textbook of Experimental Surgery.** By J. Markowitz. Pp. 527, with 330 illustrations. Baltimore, 1937, Wm. Wood and Company. \$7.

With the exception of a few facetious remarks which are of doubtful value in any scientific textbook, this work has been well done. The author has emphasized the physiologic aspects of surgery. He has also noted many advances in surgery which have developed through animal experimentation. Various procedures which have developed in the laboratory of surgical experimentation have been well described, some of which are now almost classical. The technique of operations upon animals has been thoroughly discussed and its relationship to human surgery considered. The entire book fills a very valuable place in surgery and should be in every laboratory of experimental surgery. It should be particularly valuable as a text for beginners in experimental work when any type of animal surgery is contemplated. It is an excellent book of its kind and favorably recommended.

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**Post-Graduate Surgery, Volume III.** Edited by Rodney Maingot. Cloth. Pp. 5,584, with 1,015 illustrations. New York, 1937, D. Appleton-Century Company (printed in Great Britain). Three volumes sold only as set at \$45.

The final huge tome (Volume III) of *Post-Graduate Surgery*, edited by Rodney Maingot, contains material upon a variety of topics. In sequence, the following constitute the subject matter of this book: medical aspects of surgery, hernia, plastic, obstetric, and cardiovascular surgery; lymphatic system, orthopedics, eye, ear, nose, endoscopic methods in surgery, malignant tumors of the pharynx and larynx, tonsils and adenoids, and retropharyngeal abscess, tongue, mouth and lips, esophagus and diaphragm, mandible, teeth, venereal disease, physical medicine, deep x-ray therapy, some aspects of general surgery, and finally some neurological and psychiatric aspects of surgery.

The sections on hernia by Ogilvie, on plastic surgery by Kilner, and on cardiovascular surgery by Cokkinis in which the operative procedure of Beck for coronary sclerosis is reviewed, the chapter by Sampson-Handle on the dissemination of malignant disease, and the sections on malignant tumors of the pharynx and larynx by Colledge, on tongue, mouth and lips by Cade, and that of O'Shaughnessy on the esophagus and diaphragm are easily among the better portions of the book and contain the newest and most authoritative expressions available upon these subjects. A brief but interesting and useful chapter is that of Manson-Bahr concerning elephantiasis. Medical opinion has apparently reversed itself upon the role of filaria in the occurrence of elephantiasis. A decade ago it was stated frequently that elephantiasis occurred only in the course of filariasis when streptococcal infection supervened. The experiments of Drinker and Field which indicate the susceptibility of lymphedematous tissues to infection lend increased credence to the original belief that the filaria obstructed the lymph vessels.

The chapters on the lymph vessels and their diseases by the editor, Maingot, appear to contain some unnecessary duplications of effort. Maingot emphasizes the

importance of surgery in the treatment of tuberculous lymph nodes, a practice which fell almost into disuse while roentgen treatment had its inning. The inclusion of chapters totaling almost three hundred pages on the eye, ear, and nose would indicate that the volume was probably intended for the general practitioner who does some surgery. For in this country, at any rate, the general surgeon rarely, if ever, meanders into these provinces of the surgical specialists. Many sections of the book have ample lists of excellent references which enhance the value of the work to those who seek more information upon the subjects under discussion. A detailed index facilitates access to the somewhat unrelated subject matter of the volume.

Books serve a variety of purposes. The greatest worth of this volume would seem to be as a ready reference manual to a great variety of subjects. The general surgeon will meet in it some authors who have made their reputations and others who have theirs still to make. However useful the volume may be in our day, it would take a venturesome prophet to predict that it will be read as long as Dennis', V. Bergman's, or Keen's systems of surgery, which serve many yet as important sources of helpful reference.

**Praktikum der Chirurgie.** By Professor O. Nordmann. Ed. 4. Paper. Pp. 811, with 409 illustrations. Berlin, 1938, Urban & Schwarzenberg. 25 R.M.

The purpose of the author in writing this text on the practice of surgery is to reach essentially the general practitioner who must know what surgery can offer a patient, even though he does not undertake performance of operation. The whole range of surgery is discussed in this volume exclusive of the eye and ear and *gynecologic surgery*. The clinical picture of disease entities is described with care and in detail. The indications for operation are discussed as well as choice of procedure. The technique of the more commonly performed operations is described briefly in a special section.

The author expresses, in the main, a rather conservative attitude concerning the management of most surgical disorders. The strength of the text lies in the extensive clinical and operative experience of the author; its chief weakness in that it is written by a single author, whose interest and experience of necessity cannot extend equally into all the manifold ramifications of surgery. The insertion of pertinent bibliographic references would have enhanced the value of the text. The arrangement of the subject matter could have been greatly improved upon by inserting descriptions of the operative procedure under their proper captions instead of adding them as an appendix to the text.

The author of this manual of surgery is obviously a thoughtful, critical, and practical man of large experience in the broad field of general surgery whose opinions concerning the management of surgical disorders merit justly the attention of the audience to which the book is especially directed.

**Innere Sekretion und Chirurgie.** By Hans Hanke. Pp. 326, with 18 illustrations. Berlin, 1937, Julius Springer, 23M.

This book by Hanke is an attempt to present the surgical aspects of the glands of internal secretion. There is presented in considerable detail a survey of present knowledge with respect to the physiology of these glands, a discussion of the *symptomatology* and pathogenesis of syndromes attributable to deficient and excess function, and a discussion of the possibilities of surgical intervention. In general the discussion is reasonably complete and the analysis critical and in line with conservative opinion.

The first third of the book deals with the physiology and pathology of the thyroid gland, and there follows in order a similar discussion of the parathyroids, thymus, islets of Langerhans of the pancreas, the adrenals, hypophysis, and the sex glands.

The undertaking is ambitious, and it is probable that no one man is competent to present an up-to-date analysis of the vast amount of work that is being done in the field of endocrinology. There are numerous references to the literature, and the German contributions to this field are fairly well summarized. American contributions have received relatively slight attention. This is unfortunate since most of the significant contributions in the field of endocrinology in recent years have come from American laboratories.

The printing is excellent, but the paper binding detracts somewhat from the appearance and usefulness of the volume.

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**Chemistry of the Brain.** By Irvine H. Page. Pp. 444. Springfield, Ill., 1937, Charles C. Thomas, Publisher.

At a time when interest in problems pertaining to diseases of the nervous system is being revived on a broad scale, this book is a particularly welcome addition to the much too meager literature on the subject. In his comprehensive review the author, himself an active investigator in the field, has brought together pertinent data from widely scattered sources. Contrary to what might be expected from the title, the book is not a mere compilation of facts concerning the chemical composition of the brain, but treats the subject also from the broad biochemical and physiologic viewpoints. The material has been so well selected and appraised that it will serve as a useful reference for any worker requiring orientation in the field of brain metabolism, both in health and in disease.

The first chapter of the book is appropriately devoted to the life and works of Thudichum (1828-1901), "father of brain chemistry," and the older literature on analysis of the brain. Chapters then follow on each of the major chemical constituents of nervous tissue. Because of their unique prominence in such tissue, the lipids are given first place, in spite of the fact that little is definitely known regarding their specific physiologic rôles. Separate chapters are devoted to the sterols, the phosphatides, and the fatty acids. The cerebroside is treated briefly in a special chapter. A much more extensive discussion of the carbohydrates of the brain and their intermediary metabolism is then presented. This is an especially valuable chapter because it touches upon many of the most vital problems of cerebral metabolism in health and disease. Discussion of the nitrogenous metabolism of the brain is confined to a consideration of those phases of the general subject of protein metabolism which are specially applicable to nervous tissue. While such nitrogenous metabolites as creatine, creatinine, choline, phosphagen, glutathione, and certain of the amino acids are undoubtedly of great importance in brain activity, it is pointed out that our knowledge of their exact significance is very meager. The physiologic and clinical significance of the electrolyte and gaseous metabolism of the brain is reviewed very thoroughly. The water metabolism of the brain is considered in a special chapter on physical and colloidal chemistry. Such topics as those pertaining to brain edema, water intoxication, epilepsy, and narcosis are included. In a chapter on the enzymes of the brain the author summarizes literature concerning variations in their content and activity in health and in certain diseases of the central nervous system.

Valuable miscellaneous data are assembled under the heading of comparative and developmental neurochemistry. Variations in the composition of brain tissue with age appear to have important clinical implications. The chapter on pathologic

gaseous metabolism and that on degeneration of the nervous system, as related to disturbances in nutrition, are of particular interest from the clinical point of view. Supplementing his own abbreviated discussions of brain metabolism in connection with the various topics already referred to, the author appends a special chapter by Quastel on oxidations in the brain. Data contained therein are very fundamental and are of great significance to brain physiology and pathology. The final chapter of the book is given over to a brief, philosophical discussion of "the brain and thought." Psychologists and philosophers may wish that this aspect of the subject could have been expanded, but the author wisely avoided treading where the "ice is too thin."

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**The Cerebrospinal Fluid.** By H. Houston Merritt and Frank Fremont Smith. Pp. 333, with 17 illustrations. Philadelphia, 1937, W. B. Saunders Company, \$5.

This is a book of over three hundred pages, based upon the study of some 20,000 cerebrospinal fluid specimens examined at the cerebrospinal fluid laboratory of the Neurological Unit of the Boston City Hospital and at the laboratory of Dr. James B. Ayer at the Massachusetts General Hospital. In addition, it contains a liberal number of references to the findings of other writers. The authors have taken pains to analyze the fluid findings only in those of their cases in which the diagnosis was well substantiated.

Short chapters are devoted to anatomy and physiology, technique, roentgenography, and methods of examination. Detailed consideration is given to chemistry and pathologic physiology and to the cerebrospinal syndromes in infections and diseases of the nervous system. The bibliography is extensive and a useful table is appended for the comparison of characteristic fluid findings in various conditions.

This is a well-written compilation, useful to the clinician and laboratory worker as a ready reference, rather than a presentation of new or particularly original material.

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VOLUME 3

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# INDEX TO VOLUME 3

## AUTHORS INDEX\*

In this index following the author's name the title of the subject is given as it appeared in the Journal. Editorials are also included in the list and are indicated by (E).

### A

- ALLEN, FREDERICK M. Ligation and refrigeration of intestine, 893
- ANDERSON, O. L., AND HARMOS, OSCAR. Lymphopathia venereum: treatment with diluted Frei antigen intradermally and observations on diagnosis, 41
- ATKINSON, F. R. B. (*See* Wakeley and Atkinson), 8

### B

- BAKER, DAN D. (*See* Veal and Baker), 585
- BARROW, DAVID W. (*See* Faxon and Barrow), 518
- BARTLETT, WILLARD, JR. The rôle of the liver in thyrotoxicosis, 261 (E)
- BASSLER, ANTHONY. The importance of hematemesis accompanied by pyloric obstruction, 568
- BATSON, OSCAR V. The anatomy of gall-bladder incisions, 871
- BEHREND, ALBERT, AND GRAY, HOWARD K. Acute cholecystitis, 195
- BIETER, RAYMOND N. Report on the meetings of the American Society for Pharmacology and Experimental Therapeutics, Baltimore, Md., March 30—April 2, 1938, 954
- BLALOCK, ALFRED. (*See* Levy and Blalock), 899
- BOLLMAN, JESSE L. (*See* McDonald, Schlotthauer, and Bollman), 904
- BOWER, JOHN O., BURNS, JOHN C., AND MENGLE, HAROLD A. The bacteriology of spreading peritonitis complicating acute perforative appendicitis, 615

- BOYDEN, EDWARD A. The extrahepatic biliary tract as a functional unit, 260 (E)
- BRUNSCHWIG, ALEXANDER. (*See* Soto, Brunswick, and Schlutz), 593
- BUCHSTEIN, HAROLD F., AND LOVE, J. GRAFTON. Spina bifida occulta, 215
- BUIE, LOUIS A., AND NESSELROD, JERROLD P. Diffuse, cavernous hemangioma of the rectum, 379
- BURNS, JOHN C. (*See* Bower, Burns, and Mengle), 645
- BUTSCH, WINFIELD L. (*See* Mayo and Butsch), 421

### C

- CARLSON, HJALMAR E. (*See* Ockerblad and Carlson), 391
- CARTER, B. NOLAND. The use of muscle flaps in the closure of chronic empyema cavities, 506
- CHAMBERLIN, GEORGE W. (*See* Pendergrass and Chamberlin), 840
- CHRISTOPHER, FREDERICK. Stenosis of the large bowel due to amebiasis, 75
- COLE, WARREN H. Noncalculous cholecystitis, 824
- Report of the Forty-Seventh Annual Meeting of the Western Surgical Association, Indianapolis, Ind., Dec. 3 and 4, 1937, 466
- COLEMAN, FRANK P. The effect of anesthesia on hepatic function, 87
- COMPERE, EDWARD L., AND GARRISON, MONROE. Osteodystrophy of unknown origin, 203

\*January, pp. 1-164; February, pp. 165-324; March, pp. 325-484; April, pp. 485-644; May, pp. 645-804; June, pp. 805-952.

- CONNELL, F. GREGORY. Partial gastrectomy in treatment of peptic ulcer, 696
- CRANDALL, L. A., JR., AND IVY, A. C. Applied physiology of liver, 815
- CREEVY, C. D. The operative treatment of hypospadias, 719
- The proper place of transurethral resection in surgery of prostate, 779 (E)
- Review of the meeting of the Association of American Medical Colleges, San Francisco, Calif., Oct. 25-27, 1937, 316
- CRILE, GEORGE, JR. Large bilateral adenofibromas of the breast, 68
- CUTLER, ELLIOTT C. Opportunities for graduate training in surgery, 424

D

- DACK, G. M. (See Haerem, Dack, and Wilson), 333
- (See Haerem, Dack, and Dragstedt), 339
- D'AUNOY, RIGNEY, OGDEN, MICHAEL ALEXANDER, AND HALPERT, BÉLA. Primary carcinoma of the biliary system, 670
- DAVIDSON, ARTHUR J. (See Horwitz and Davidson), 407
- , AND HORWITZ, M. THOMAS. Resection of the elbow joint, 226
- DAVIS, JOHN STAIGE. The operative treatment of scars following bedsores, 1
- DEBAKEY, MICHAEL. "Canned" blood transfusion, 136 (E)
- Continuous drip transfusion, 914 (E)
- DEVINE, SIR HUGH. Operation on a defunctioned distal colon, 165
- DRAGSTEDT, LESTER R. (See Haerem, Dack, and Dragstedt), 339
- DUNCAN, GEORGE A. Congenital and developmental coxa vara, 741

E

- ELOESSER, L., AND FREEMAN, ANTHONY. A model to illustrate the mechanics of respiration and movements of the mediastinum with and without various kinds and degrees of bronchial stenosis, 774

- FAXON, HENRY H., AND BARROW, DAVID W. The end-results of high ligation and injection in the treatment of varicose veins, 518
- FRAZIER, W. D. (See Ravidin, Rhoads, Frazier, and Ulin), 805
- FREEMAN, ANTHONY (See Eloesser and Freeman), 774

G

- GAGE, MIMS. Sinus tracts and their identification, 605 (E)
- GALE, JOSEPH W., AND MIDELFART, PETER A. Extrafascial apicolysis (Semb), 234
- GARRISON, MONROE. (See Compere and Garrison), 203
- GESCHICKTER, CHARLES F. Mammary tumors, 916
- GOGOL, L. J. Subphrenic abscess, 386
- GOTCHER, VERNON A. (See Pund and Gotcher), 34
- GRAHAM, EVARTS A. Some accomplishments of thoracic surgery and its present problems, 485
- GRAY, HOWARD K. (See Behrend and Gray), 195
- GURNEY, CHARLES E. Experimental study of the behavior of free fat transplants, 679

H

- HAEREM, SARAH, DACK, G. M., AND DRAGSTEDT, LESTER R. Acute intestinal obstruction. II. The permeability of obstructed bowel segments of dogs to *Clostridium botulinum* toxin, 339
- , —, AND WILSON, HARWELL. Acute intestinal obstruction. I. The rôle of bacteria in closed jejunal loops, 333
- HALE, DONALD E., AND TOVELL, RALPH M. Choice of anesthetic agents and methods of their administration for diabetic patients, 100
- HALPERT, BÉLA. Right retromesocolic hernia, 579
- (See D'Aunoy, Ogden, and Halpert), 670
- HARKINS, HENRY N. Acute ulcer of the duodenum (Curling's ulcer) as a complication of burns; relation to sepsis, 608
- Recent advances in the study of burns, 430

- HARMOS, OSCAR. (*See* Anderson and Harmos), 41
- HEBERT, WARREN H. Peptic ulcers following experimentally produced obstructive jaundice, 370
- HIBBARD, JAMES S., AND KREMEN, ARNOLD J. Effect of the volatile base in fluid intestinal contents on dogs with low intestinal obstruction, 325
- HORGAN, EDMUND. Varicose veins, with special reference to treatment by ligation, stripping, and injection, 528
- HORWITZ, M. THOMAS. (*See* Davidson and Horwitz), 226
- , AND DAVIDSON, ARTHUR J. Newer concepts in the treatment of injuries to the ligaments of the knee joint; an evaluation of the Mauck operation, 407

## I

- IVY, A. C. (*See* Crandall, Jr., and Ivy), 815

## J

- JOHNSTON, C. G. Preoperative and post-operative treatment in cases of obstructive jaundice, 875
- JUNG, ADOLPHE. Review of the Forty-Sixth French Congress of Surgery, Oct. 4-9, 1937, Paris, 306

## K

- KERN, HOWARD M. Carcinoma of jejunum, 556
- KREMEN, ARNOLD J. (*See* Hibbard and Kremen), 325

## L

- LAWTON, STANLEY E. Bone metastases from carcinoma of the stomach, 121
- LEHMAN, EDWIN P. Is judgment necessarily inarticulate? 427 (*E*)
- LEVEN, N. L. (*See* Peyton and Leven), 702
- LEVY, SANFORD E., AND BLALOCK, ALFRED. Experimental attempts to prevent or abolish the hypertension that is associated with renal ischemia, 899
- LITZENBERG, JENNINGS C. The Centennial Meeting of the American Association of Obstetricians,

## LITZENBERG—Cont'd

- Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 20-22, 1937, 319
- LOVE, J. GRAFTON. (*See* Buchstein and Love), 215

## M

- MAHORNER, HOWARD R. Review of the Southern Surgical Association meeting, Dec. 7-9, 1937, Birmingham, Ala., 470
- MARTIN, H. E., AND TRUSLER, H. M. The cause of death in liver peritonitis, 58
- MAYO, CHARLES W., AND BUTSCH, WINFIELD L. Rectovaginal cloaca, 421
- MCCORKLE, HORACE, AND STEVENSON, JEAN. Psoas abscess of the appendix, 574
- MCDONALD, JOHN R., SCHLOTTHAUER, CARL F., AND BOLLMAN, JESSE L. The pathogenesis of seminoma of the testis, 904
- MENGLE, HAROLD A. (*See* Bower, Burns, and Mengle), 645
- MIDELFART, PETER A. (*See* Gale and Midelfart), 234
- MILCH, HENRY. Treatment of dislocation of the shoulder, 732
- MOORE, ROBERT M. Some experimental observations relating to visceral pain, 534

## N

- NESSERLOD, JERROLD P. (*See* Buie and Nesselrod), 379

## O

- OCHSNER, ALTON. Abdominal wall susceptibility to infection, 783 (*E*)
- OCKERBLAD, NELSE F., AND CARLSON, HJALMAR E. Urethral urinary extravasation, 391
- OGDEN, MICHAEL ALEXANDER. (*See* D'Aunoy, Ogden, and Halpert), 670

## P

- PAINE, J. RANDOLPH, AND RIGLER, LEO G. Pneumoperitoneum in perforations of the gastrointestinal tract, 351
- PEMBERTON, JOHN DEL., AND STALKER, LEONARD K. Meckel's diverticulum, 563

- PENDERGRASS, EUGENE P., AND CHAMBERLIN, GEORGE W. Roentgen diagnosis of surgical diseases of the liver and biliary tract, 840
- PEYTON, W. T., AND LEVEN, N. L. Hemangioma and its treatment, 702
- POWERS, JOHN H. Concerning renal function and structure following trauma of the kidney, 397
- PUND, EDGAR R., AND GOTCHER, VERNON A. Granuloma venereum (granuloma inguinale) of uterus, tubes, and ovaries, 34
- R
- RAVDIN, I. S. Recent advances in our knowledge of biliary function, 912 (E)
- , RHOADS, J. E., FRAZIER, W. D., AND ULIN, A. W. The effect of recent advances in biliary physiology on the mortality following operation for common duct obstruction, 805
- REA, CHARLES E. The hormonal basis of the etiology and treatment of prostatic hypertrophy, 138
- REICH, RUDOLPH S. Posterior dislocation of the first cervical vertebra with fracture of the odontoid process, 416
- REID, MONT R. The appendicitis problem, 601 (E)
- RHOADS, J. E. (See Ravdin, Rhoads, Frazier, and Ulin), 805
- RIENHOFF, WILLIAM F., JR. The surgical treatment of carcinoma of the breast, 133 (E)
- RIGLER, LEO G. Report of the meeting of the Fifth International Congress of Radiology in Chicago, Ill., 157
- (See Paine and Rigler), 351
- ROTHENBERG, ROBERT E. (See Wolfson and Rothenberg), 663
- RUSH, H. LOWRY. (See Rush and Rush), 200
- RUSH, LESLIE V., AND RUSH, H. LOWRY. A reconstruction operation for diastasis recti, 200
- S
- SARNOFF, JACOB. Cancer of the breast in the male, 766
- SCHLOTTHAUER, CARL F. (See McDonald, Schlotthauer, and Bollman), 904
- SOHLUTZ, F. W. (See Soto, Brunswick, and Schlutz), 593
- SEARLS, HENRY H. Review of the thirteenth annual meeting of the Pacific Coast Surgical Association, Los Angeles, Calif., Feb. 22-25, 1938, 950
- SEEGER, STANLEY J. Congenital arteriovenous anastomoses, 264
- SEMB, CARL. Report of the proceedings of the Surgical Congress at Gothenburg, June 28-30, 1937, 149
- SHELLEY, HAROLD J. Calcified fecalith in the appendix, 658
- STRAUSS, A., AND TOMARKIN, JOSEPH. Acute appendicitis, 111
- SOTO, JOSE A., BRUNSCHWIG, ALEXANDER, AND SCHLUTZ, F. W. An experimental study of the effects of x-radiation upon acute pyogenic infection of the skin and subcutaneous tissues, 593
- STALKER, LEONARD L. (See Pemberton and Stalker), 563
- STEVENSON, JEAN. (See McCorkle and Stevenson), 574
- SWEENEY, H. MORROW. The effect of carbon arc radiation on wound healing, 127
- T
- TOMARKIN, JOSEPH (See Strauss and Tomarkin), 111
- TOVELL, RALPH M. (See Hale and Tovell), 100
- TRUSLER, H. M. (See Martin and Trusler), 58
- TUOHY, EDWARD B. Meeting of the Anesthetists' Travel Club, Montreal and Toronto, Oct. 18-23, 1937, 156
- U
- ULIN, A. W. (See Ravdin, Rhoads, Frazier, and Ulin), 805
- V
- VEAL, J. ROSS, AND BAKER, DAN D. Repair of direct inguinal hernia by osteoperiosteal graft to the pectineal line of the pubis, 585
- W
- WAKELEY, CECIL P. G., AND ATKINSON, F. R. B. Acromegaly, 8

- WALTERS, WALTMAN. Personal experiences in the treatment of benign obstructing lesions of the biliary tract, 884
- , Recent advances in the surgical treatment of lesions of the biliary tract, 786
- WEINBERG, JOSEPH. Diaphragmatic hernia in infants; surgical treatment with use of renal fascia, 78
- WELCH, CLAUDE E. A method of constant suction applied to the Levine tube, 693
- WILENSKY, ABRAHAM O. Osteomyelitis of the scapula, 21
- WILSON, HARWELL (*See* Haerem, Dack, and Wilson), 333
- WOLFSON, WILLIAM L., AND ROTHENBERG, ROBERT E. The surgical treatment of complicated duodenal ulcer, 663

# SUBJECT INDEX\*

Book reviews are indicated by (B. Rev.) after the page number; editorials, by (E) after the page number.

## A

- Abdominal wall susceptibility to infection (Ochsner), 783 (E)
- Abscess, psoas, of appendix (McCorkle and Stevenson), 574
  - subphrenic (Gogol), 386
- Acromegaly (Wakeley and Atkinson), 8
- Adenofibromas, large, bilateral, of breast (Crile, Jr.), 68
- Amebiasis, stenosis of large bowel due to (Christopher), 75
- American Association of Obstetricians, Gynecologists and Abdominal Surgeons, centennial meeting of, Hot Springs, Va., Sept. 20-22, 1937 (Litzenberg), 319
  - Society for Pharmacology and Experimental Therapeutics, report on meetings of, Baltimore, Md., March 30—April 2, 1938 (Bieter), 954
- Anastomoses, congenital arteriovenous (Seeger), 264
- Anatomy of gall-bladder incisions (Battson), 871
- Anesthesia, effect of, on hepatic function (Coleman), 87
- Anesthetic agents, choice of, and methods of administration for diabetic patients (Hale and Tovell), 100
- Anesthetists' Travel Club, meeting of, Montreal and Toronto, Oct. 18-23, 1937 (Tuohy), 156
- Antigen, Frei, diluted, intradermally, treatment of lymphopathia venereum with (Anderson and Harnos), 41
- Apicolysis, extrafascial (Semb) (Gale and Midelfart), 234
- Appendicitis, acute (Strauss and Tomarkin), 111
  - perforative, bacteriology of spreading peritonitis complicating (Bower, Burns, and Mengle), 645
  - problem (Reid), 601 (E)
- Appendix, calcified fecolith in (Shelley), 658
  - psoas abscess of (McCorkle and Stevenson), 574
- Arteriovenous anastomoses, congenital (Seeger), 264
- Association of American Medical Colleges, review of meeting of, San Francisco, Calif., Oct. 25-27, 1937 (Creedy), 316

Atlas of skeletal maturation, 642 (B. Rev.)

## B

- Bacteria, rôle of, in closed jejunal loops, in acute intestinal obstruction (Haerem, Dack, and Wilson), 333
- Bacteriology of spreading peritonitis complicating acute perforative appendicitis (Bower, Burns, and Mengle), 645
- Bedsore, operative treatment of scars following (Davis), 1
- Benign obstructing lesions of biliary tract, personal experiences in treatment of (Walters), 884
- Biliary disease, symposium on, 805-892
  - function, recent advances in our knowledge of (Ravdin), 912 (E)
  - physiology, effect of recent advances in, on mortality following operation for common duct obstruction (Ravdin, Rhoads, Frazier, and Ulin), 805
  - system, primary carcinoma of (D'Aunoy, Ogden, and Halpert), 670
  - tract, benign obstructing lesions of, personal experiences in treatment of (Walters), 884
    - extrahepatic, as functional unit (Boyden), 260 (E)
    - lesions of, recent advances in surgical treatment of (Walters), 786
    - and liver, roentgen diagnosis of surgical diseases of (Pendergrass and Chamberlin), 840
- Blood transfusion, "canned" (DeBakey), 136 (E)
- Bone metastases from carcinoma of stomach (Lawton), 121
- Bowel, large, stenosis of, due to amebiasis (Christopher), 75
  - segments, obstructed, of dogs, permeability of, to *Cl. botulinum* toxin (Haerem, Dack, and Dragstedt), 339
- Breast, cancer of, in male (Sarnoff), 766
  - carcinoma of, surgical treatment of (Rienhoff, Jr.), 133 (E)
  - large bilateral adenofibromas of (Crile, Jr.), 63

\*January, pp. 1-164; February, pp. 165-324; March, pp. 325-481; April, pp. 482-644; May, pp. 645-801; June, pp. 802-972.

- Brief outline of modern treatment of fractures, 322 (B. Rev.)
- Bronchial stenosis, model to illustrate mechanics of respiration and movements of mediastinum with and without various kinds and degrees of (Eloesser and Freeman), 774
- Burns, acute ulcer of duodenum as complication of (Harkins), 608  
recent advances in study of (Harkins), 430

## C

- "Canned" blood transfusion (DeBakey), 136 (E)
- Cancer of breast in male (Sarnoff), 766
- Carcinoma of breast, surgical treatment of (Rienhoff, Jr.), 133 (E)  
of jejunum (Kern), 556  
primary, of biliary system (D'Aunoy, Ogden, and Halpert), 670  
of stomach, bone metastases from (Lawton), 121
- Carbon arc radiation, effect of, on wound healing (Sweeney), 127
- Cavities, chronic empyema, use of muscle flaps in closure of (Carter), 506
- Cerebrospinal fluid, 960 (B. Rev.)
- Cervical vertebra, first, posterior dislocation of, with fracture of odontoid process (Reich), 416
- Chemistry of the brain, 959 (B. Rev.)
- Cholecystitis, acute (Behrend and Gray), 195  
noncalculous (Cole), 824
- Cloaca, rectovaginal (Mayo and Butsch), 421
- Clostridium botulinum* toxin, permeability of obstructed bowel segments of dogs to (Haerem, Dack, and Dragstedt), 339
- Common duct obstruction, mortality following operation for, effect of recent advances in biliary physiology on (Ravdin, Rhoads, Frazier, and Ulin), 805
- Collapse theory of pulmonary tuberculosis, 482 (B. Rev.)
- Collected papers of the Mayo Clinic and Mayo Foundation, vol. XXVIII, 1936, 481 (B. Rev.)
- Colon, defunctioned distal, operation on (Devine), 165
- Congenital arteriovenous anastomoses (Seeger), 261  
and developmental coxa vara (Duncan), 741
- Continuous drip transfusion (DeBakey), 914 (E)
- Coxa vara, developmental and congenital (Duncan), 741
- Curling's ulcer as complication of burns (Harkins), 608

## D

- Defunctioned distal colon, operation on (Devine), 165
- Demonstrations of physical signs in clinical surgery, 803 (B. Rev.)
- Diabetic patients, choice and methods of administration of anesthetic agents for (Hale and Tovell), 100
- Diagnostisch—Therapeutische Technik für den Chirurgen, 642 (B. Rev.)
- Diaphragmatic hernia in infants; surgical treatment with use of renal fascia (Weinberg), 78
- Diastasis recti, reconstruction operation for (Rush and Rush), 200
- Disease, biliary, symposium on, 805-892
- Diseases of the nervous system in infancy, childhood and adolescence, 479 (B. Rev.)  
surgical, of liver and biliary tract, roentgen diagnosis of (Pendergrass and Chamberlin), 840
- Dislocation, posterior, of first cervical vertebra with fracture of odontoid process (Reich), 416  
of shoulder, treatment of (Milch), 732
- Distal colon, defunctioned, operation on (Devine), 165
- Diverticulum, Meckel's (Pemberton and Stalker), 563
- Drip transfusion, continuous (DeBakey), 914 (E)
- Duodenal ulcer, complicated, surgical treatment of (Wolfson and Rothenberg), 663
- Duodenum, acute ulcer of, as complication of burns (Harkins), 608

## E

- Elbow joint, resection of (Davidson and Horwitz), 226
- Elements of orthopaedic surgery, 643 (B. Rev.)
- Empyema cavities, chronic, use of muscle flaps in closure of (Carter), 506
- Extrascapular apicolysis (Semb) (Gale and Midelfart), 234
- Extrahepatic biliary tract as functional unit (Boyden), 260 (E)
- Extravasation, urethral, urinary (Ockerblad and Carlson), 391

## F

- Fascia, renal, surgical treatment of diaphragmatic hernia in infants with use of (Weinberg), 78
- Fat transplants, free, experimental study of behavior of (Gurney), 679
- Fecalith, calcified, in appendix (Shelley), 658



- Flaps, muscle, use of, in closure of chronic empyema cavities (Carter), 506
- Fracture of odontoid process, posterior dislocation of first cervical vertebra with (Reich), 416
- Frei antigen, diluted, intradermally, treatment of lymphopathia venereum with (Anderson and Harnos), 41
- French Congress of Surgery, forty-sixth, Oct. 4-9, 1937, Paris, review of (Jung), 306
- Function, biliary, recent advances in our knowledge of (Ravdin), 912 (E)
- hepatic, effect of anesthesia on (Coleman), 87
- G**
- Gall-bladder incision, anatomy of (Batson), 871
- Gastrectomy, partial, in treatment of peptic ulcer (Connell), 696
- Gastrointestinal tract, perforations of, pneumoperitoneum in (Paine and Rigler), 351
- Genital abnormalities, hermaphroditism and related genital abnormalities, 479 (B. Rev.)
- Graduate training in surgery, opportunities for (Cutler), 424 (E)
- Graft, osteoperiosteal, to pectineal line of pubis, repair of direct inguinal hernia by (Veal and Baker), 585
- Granuloma inguinale of uterus, tubes, and ovaries (Pund and Gotcher), 34
- venereum of uterus, tubes, and ovaries (Pund and Gotcher), 34
- H**
- Healing, wound, effect of carbon arc radiation on (Sweeney), 127
- Hemangioma, diffuse, cavernous, of rectum (Buie and Nesselrod), 379 and its treatment (Peyton and Leven), 702
- Hematemesis accompanied by pyloric obstruction, importance of (Basler), 568
- Hepatic function, effect of anesthesia on (Coleman), 87
- Hernia, diaphragmatic, in infants; surgical treatment with use of renal fascia (Weinberg), 78
- direct inguinal, repair of, by osteoperiosteal graft to pectineal line of pubis (Veal and Baker), 585
- right retromesocolic (Halpert), 579
- Hormonal basis of etiology and treatment of prostatic hypertrophy (Rea), 138
- Hypertension associated with renal ischemia, experimental attempts to prevent or abolish (Levy and Blalock), 899
- Hypertrophy, prostatic, hormonal basis of etiology and treatment of (Rea), 138
- Hypospadias, operative treatment of (Creery), 719
- I**
- Incisions, gall-bladder, anatomy of (Batson), 871
- Infection, abdominal wall susceptibility to (Ochsner), 783 (E)
- acute pyogenic, of skin and subcutaneous tissues, experimental study of effects of x-radiation upon (Soto, Brunswick, and Schlutz), 593
- Inguinal hernia, direct, repair of, by osteoperiosteal graft to pectineal line of pubis (Veal and Baker), 585
- Injection and high ligation, end-results of, in treatment of varicose veins (Faxon and Barrow), 518
- ligation, and stripping, treatment of varicose veins by (Horgan), 528
- Innere Sekretion und Chirurgie, 958 (B. Rev.)
- International Congress of Radiology, fifth, report of meeting of, Chicago, Ill. (Rigler), 157
- Intestinal contents, fluid, effect of volatile base in, on dogs with low intestinal obstruction (Hibbard and Kremen), 325
- obstruction, acute; I. rôle of bacteria in closed jejunal loops (Haerem, Dack, and Wilson), 333
- II. permeability of obstructed bowel segments of dogs to *Cl. botulinum* (Haerem, Dack, and Dragstedt), 339
- low, effect of volatile base in fluid intestinal contents on dogs with (Hibbard and Kremen), 325
- Intestine, ligation and refrigeration of (Allen), 893
- Infants, diaphragmatic hernia in; surgical treatment of, with use of renal fascia (Weinberg), 78
- Ischemia, renal, experimental attempts to prevent or abolish hypertension associated with (Levy and Blalock), 899
- J**
- Jaundice, obstructive, experimentally produced, peptic ulcers following (Hebert), 370
- preoperative and postoperative treatment in cases of (Johnston), 575

Jejunal loops, closed, rôle of bacteria in, in acute intestinal obstruction (Haerem, Dack, and Wilson), 333

Jejunum, carcinoma of (Kern), 556

Joint, elbow, resection of (Davidson and Horwitz), 226

knee, treatment of injuries to ligaments of (Horwitz and Davidson), 407

Judgment, is it necessarily inarticulate? (Lehman), 427 (E)

## K

Kidney, trauma of, renal function and structure following (Powers), 397

Knee joint, treatment of injuries to ligaments of (Horwitz and Davidson), 407

## L

Laboratory diagnosis of syphilis, 802 (B. Rev.)

Legal medicine and toxicology, 801 (B. Rev.)

Lehrbuch der Kriegs Chirurgie, 801 (B. Rev.)

Les methodes chirurgicales de traitement de l'angine de poitrine. Evolution et resultats, 799 (B. Rev.)

Lesions, benign obstructing, of biliary tract, personal experiences in treatment of (Walters), 884

of biliary tract, treatment of, recent advances in (Walters), 786

Levine tube, method of constant suction applied to (Welch), 693

Ligaments of knee joint, treatment of injuries to (Horwitz and Davidson), 407

Ligation, high, and injection, end-results of, in treatment of varicose veins (Faxon and Barrow), 518 and refrigeration of intestine (Allen), 893

stripping, and injection, treatment of varicose veins by (Horgan), 528

Liver, applied physiology of (Crandall, Jr., and Ivy), 815

and biliary tract, surgical diseases of, roentgen diagnosis of (Pendergrass and Chamberlin), 840

peritonitis, cause of death in (Martin and Trusler), 58

rôle of, in thyrotoxicosis (Bartlett, Jr.), 261 (E)

Loops, closed jejunal, rôle of bacteriology in, in acute intestinal obstruction (Haerem, Dack, and Wilson), 333

Lymphopathia venereum, treatment with diluted Frei antigen intradermally and observations on diagnosis (Anderson and Harms), 41

## M

Male, cancer of breast in (Sarnoff), 766

Mammary tumors (Geschickter), 916

Mauck operation, evaluation of, treatment of injuries to ligaments of knee joint (Horwitz and Davidson), 407

Meckel's diverticulum (Pemberton and Stalker), 563

Mediastinum, movements of, model to illustrate (Eloesser and Freeman), 774

Megacolon und Megacystis, 644 (B. Rev.)

Metastases, bone, from carcinoma of stomach (Lawton), 121

Mortality following operation for common duct obstruction, effect of recent advances in biliary physiology on (Ravdin, Rhoads, Frazier, and Ulin), 805

Muscle flaps, use of, in closure of chronic empyema cavities (Carter), 506

## N

Neurology, 483 (B. Rev.)

Noncalculous cholecystitis (Cole), 824

## O

Obstruction, acute intestinal; I. rôle of bacteria in closed jejunal loops (Haerem, Dack, and Wilson), 333

II. permeability of obstructed bowel segments of dogs to *Cl. botulinum* (Haerem, Dack, and Dragstedt), 339

common duct, mortality following operation for, effect of recent advances in biliary physiology on (Ravdin, Rhoads, Frazier, and Ulin), 805

low intestinal, effect of volatile base in fluid intestinal contents on dogs with (Hibbard and Kremen), 325

pyloric, importance of hematemesis accompanied by (Bassler), 568

Obstructing lesions, benign, of biliary tract, personal experiences in treatment of (Walters), 884

Obstructive jaundice, experimentally produced, peptic ulcers following (Hebert), 370

preoperative and postoperative treatment in cases of (Johnston), 875

Odontoid process, fracture of, posterior dislocation of first cervical vertebra with (Reich), 416

Operation for common duct obstruction, mortality following, effect of recent advances in biliary physiology on (Ravdin, Rhoads, Frazier, and Ulin), 805

## Operation—Cont'd

- Mauck, evaluation of, in treatment of injuries to ligaments of knee joint (Horwitz and Davidson), 407
- Operative surgery, 193 (B. Rev.)  
the ear, air passages and neck, 643 (B. Rev.)
- Osteodystrophy of unknown origin (Compere and Garrison), 203
- Osteomyelitis of scapula (Wilensky), 21
- Osteoperiosteal graft to pectineal line of pubis, repair of direct inguinal hernia by (Veal and Baker), 585
- Ovaries, granuloma venereum (granuloma inguinale) of (Pund and Gotcher), 34

## P

- Pacific Coast Surgical Association, review of thirteenth annual meeting, Los Angeles, Calif., Feb. 22-25, 1938 (Searls), 950
- Pain, visceral, some experimental observations relating to (Moore), 534
- Patients, diabetic, choice and methods of administration of anesthetic agents for (Hale and Tovell), 100
- Pathogenesis of seminoma of testis (McDonald, Schlotthauer, and Bollman), 904
- Pectineal line of pubis, repair of direct inguinal hernia by osteoperiosteal graft to (Veal and Baker), 585
- Peptic ulcers following experimentally produced obstructive jaundice (Hebert), 370  
treatment of, partial gastrectomy in (Connell), 696
- Peritonitis, liver, cause of death in (Martin and Trusler), 58  
spreading, complicating acute perforative appendicitis (Bower, Burns, and Mengle), 645
- Physiology, applied, of liver (Crandall, Jr., and Ivy), 815  
biliary, effect of recent advances in, on mortality following operation for common duct obstruction (Ravdin, Rhoads, Frazier, and Ulin), 805
- Pneumoperitoneum in perforations of gastrointestinal tract (Paine and Rigler), 351
- Post-graduate surgery, vol. III, 957 (B. Rev.)
- Postmortem examination, 802 (B. Rev.)
- Postoperative and preoperative treatment in cases of obstructive jaundice (Johnston), 875
- Practical proctology, 804 (B. Rev.)
- Praktikum der Chirurgie, 958 (B. Rev.)

- Preoperative and postoperative treatment in cases of obstructive jaundice (Johnston), 875
- Prostate, surgery of, proper place of transurethral resection in (Creery), 779 (E)
- Prostatic hypertrophy, hormonal basis of etiology and treatment of (Rea), 138
- Psoas abscess of appendix (McCorkle and Stevenson), 574
- Pubis, pectineal line of, repair of direct inguinal hernia by periosteal graft to (Veal and Baker), 585
- Pyogenic infection, acute, of skin and subcutaneous tissues, experimental study of effects of x-radiation upon (Soto, Brunschwig, and Schlutz), 593
- Pyloric obstruction, importance of hematemesis accompanied by (Bassler), 568

## R

- Radiation, carbon arc, effect of, on wound healing (Sweeney), 127
- Reconstruction operation for diastasis recti (Rush and Rush), 200
- Recti, diastasis, reconstruction operation for (Rush and Rush), 200
- Rectovaginal cloaca (Mayo and Butsch), 421
- Rectum, diffuse, cavernous hemangioma of (Buie and Nesselrod), 379
- Refrigeration and ligation of intestine (Allen), 893
- Renal fascia, surgical treatment of diaphragmatic hernia in infants with use of (Weinberg), 78  
function and structure, following trauma of kidney (Powers), 397  
ischemia, experimental attempts to prevent or abolish hypertension associated with (Levy and Blacklock), 899
- Resection of elbow joint (Davidson and Horwitz), 226  
transurethral, proper place of, in surgery of prostate (Creery), 779 (E)
- Respiration, mechanics of, model to illustrate (Eloesser and Freeman), 774
- Retromesocolic hernia, right (Halpert), 579
- Röntgen diagnosis of surgical diseases of liver and biliary tract (Pendergrass and Chamberlin), 840

## S

- Scapula, osteomyelitis of (Wilensky), 21
- Sears, operative treatment of, following bedsores (Davis), 1
- Seminoma of testis, pathogenesis of (McDonald, Schlotthauer, and Bollman), 904

- Sepsis, relation to, acute ulcer of duodenum as complication of burns (Harkins), 608
- Shoulder, dislocation of, treatment of (Milch), 732
- Sinus tracts and their identification (Gage), 605 (*E*)
- Skin and subcutaneous tissues, acute pyogenic infection of, experimental study of effects of x-radiation upon (Soto, Brunschwig, and Schlutz), 593
- Southern Surgical Association, review of meeting of, Dec. 7-9, 1937, Birmingham, Ala. (Mahorner), 470
- Spina bifida occulta (Buchstein and Love), 215
- Stenosis, bronchial, model to illustrate mechanics of respiration with and without various degrees of (Eloesser and Freeman), 774  
of large bowel due to amebiasis (Christopher), 75
- Stomach, carcinoma of, bone metastases from (Lawton), 121
- Stripping, ligation, and injection, treatment of varicose veins by (Horgan), 528
- Subcutaneous tissues and skin, acute pyogenic infection of, experimental study of effects of x-radiation upon (Soto, Brunschwig, and Schlutz), 593
- Subphrenic abscess (Gogol), 386
- Suction, constant, method of, applied to Levine tube (Welch), 693
- Surgery, opportunities for graduate training in (Cutler), 424 (*E*)  
of prostate, proper place of transurethral resection in (Creedy), 779 (*E*)  
recent advances in, department of, 138, 264, 430, 608, 786, 916  
thoracic, and its present problems, some accomplishments of (Graham), 485
- Surgical Congress at Gothenburg, June 28-30, 1937, report of proceedings of (Semb), 149  
diseases of liver and biliary tract, roentgen diagnosis of (Pendergrass and Chamberlin), 840  
treatment, 163 (*B. Rev.*)  
of complicated duodenal ulcer (Wolfson and Rothenberg), 663  
of lesions of biliary tract, recent advances in (Walters), 786
- Symposium on biliary disease, 805-892
- Synopsis of ano-rectal diseases, 803 (*B. Rev.*)  
of digestive diseases, 161 (*B. Rev.*)  
of genito-urinary diseases, 324 (*B. Rev.*)
- T
- Testis, seminoma of, pathogenesis of (McDonald, Schlotthauer, and Bollman), 904
- Textbook of diagnostic roentgenology, 481 (*B. Rev.*)  
of experimental surgery, 957 (*B. Rev.*)
- Therapeutic problem in bowel obstruction, 480 (*B. Rev.*)
- Thoracic surgery and its present problems, some accomplishments of (Graham), 485
- Thyrototoxicosis, rôle of liver in (Bartlett, Jr.), 261 (*E*)
- Tissues, subcutaneous, and skin, acute pyogenic infections of, experimental study of effects of x-radiation upon (Soto, Brunschwig, and Schlutz), 593
- Toxin, *Cl. botulinum*, permeability of obstructed bowel segments of dogs to (Haerem, Daek, and Dragstedt), 339
- Tract, biliary, benign obstructing lesions of, personal experiences in treatment in (Walters), 884  
extrahepatic, as functional unit (Boyden), 260 (*E*)  
recent advances in surgical treatment of lesions of (Walters), 786  
gastrointestinal, pneumoperitoneum in perforations of (Paine and Rigler), 351  
sinus, and their identification (Gage), 605 (*E*)
- Training, graduate, in surgery, opportunities for (Cutler), 424 (*E*)
- Traitement chirurgical du cancer du colon pelvien, 322 (*B. Rev.*)
- Transfusion, "canned" blood (DeBakey), 136 (*E*)  
continuous drip (DeBakey), 914 (*E*)
- Transplants, free fat, experimental study of behavior of (Gurney), 679
- Transurethral resection, proper place of, in surgery of prostate (Creedy), 779 (*E*)
- Trauma of kidney, renal function and structure following (Powers), 397
- Treatment of benign obstructing lesions of biliary tract, personal experiences in (Walters), 884  
preoperative and postoperative, in cases of obstructive jaundice (Johnston), 875
- Tubes, granuloma venereum (granuloma inguinale) of (Pund and Gotcher), 34  
Levine, method of constant suction applied to (Welch), 693
- Tumors, mammary (Geschickter), 916  
of the nervous system, 323 (*B. Rev.*)

## U

- Ulcer, acute, of duodenum, as complication of burns (Harkins), 608  
 complicated duodenal, surgical treatment of (Wolfson and Rothenberg), 663  
 Curling's, as complication of burns (Harkins), 608  
 peptic, following experimentally produced obstructive jaundice (Hertbert), 370  
 treatment of, partial gastrectomy in (Connell), 696  
 Urethral urinary extravasation (Ockerblad and Carlson), 391  
 Urinary extravasation, urethral (Ockerblad and Carlson), 391  
 Uterus, granuloma venereum (granuloma inguinale) of (Pund and Gotcher), 34

## V

- Varicose veins, with special reference to treatment by ligation, stripping, and injection (Horgan), 528  
 Veins, varicose, end-results of high ligation and injection in treatment of (Faxon and Barrow), 518

## Veins, varicose—Cont'd

- with special reference to treatment by ligation, stripping, and injection (Horgan), 528  
 Vertebra, first cervical, posterior dislocation of, with fracture of odontoid process (Reich), 416  
 Visceral pain, some experimental observations relating to (Moore), 534  
 Volatile base, effect of, in fluid intestinal contents on dogs with low intestinal obstruction (Hibbard and Kremen), 325

## W

- Western Surgical Association, report of forty-seventh annual meeting of, Indianapolis, Ind., Dec. 3 and 4, 1937 (Cole), 466  
 Wound healing, effect of carbon arc radiation on (Sweeney), 127

## X

- X-radiation, experimental study of effects of, upon acute pyogenic infection of skin and subcutaneous tissues (Soto, Brunschwig and Schlutz), 593



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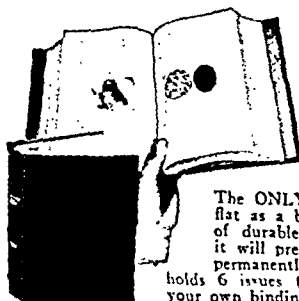
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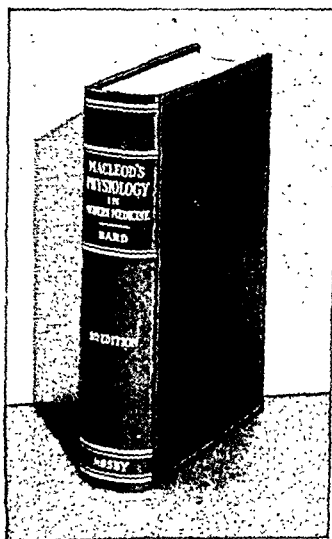
If you are to practice medicine or surgery successfully you must know the physiological function of bodily organs. Unless you have this knowledge you are groping in the dark—you are seeking to get results in a hit or miss fashion. You must be able to translate disease in terms of disturbed physiologic function and to base treatment, medical or surgical, upon the restoration of function to organs diseased.

The attention of the entire medical and surgical profession should be focused on the new physiology pictured and described on this page—the book that is the pioneer in the field of clinical physiology. A new edition of this famous work has just been published under the editorship of Dr. Philip Bard, Professor of Physiology, Johns Hopkins University. He called to his assistance in this revision outstanding colleagues from the University of Pennsylvania, Yale University, Columbia University, Harvard Medical School, and the University of California.

Brand new—and balanced in its discussion of pure physiology in its relation to clinical medicine and surgery—this work is a masterful revision of the pioneer book in clinical physiology.

## BRAND NEW

Little of the Seventh Edition remains. The greater part of the book has been entirely rewritten. Each major subdivision is the work of a writer who is actively engaged in the study of some phase of the subject he treats. The ever-increasing bulk of original literature in physiology has made it most difficult for one, or even two or three, individuals to present in adequate fashion the facts and conceptions which should be made available to students and practitioners of medicine. Further, the treatment of each subject by one who has personally launched an experimental attack in some sector of that general field is likely to result in the placing of stress on actual experimental evidence. This will tend to stimulate the reader to weigh the evidence and to achieve an understanding by the selection and coordination of significant facts.



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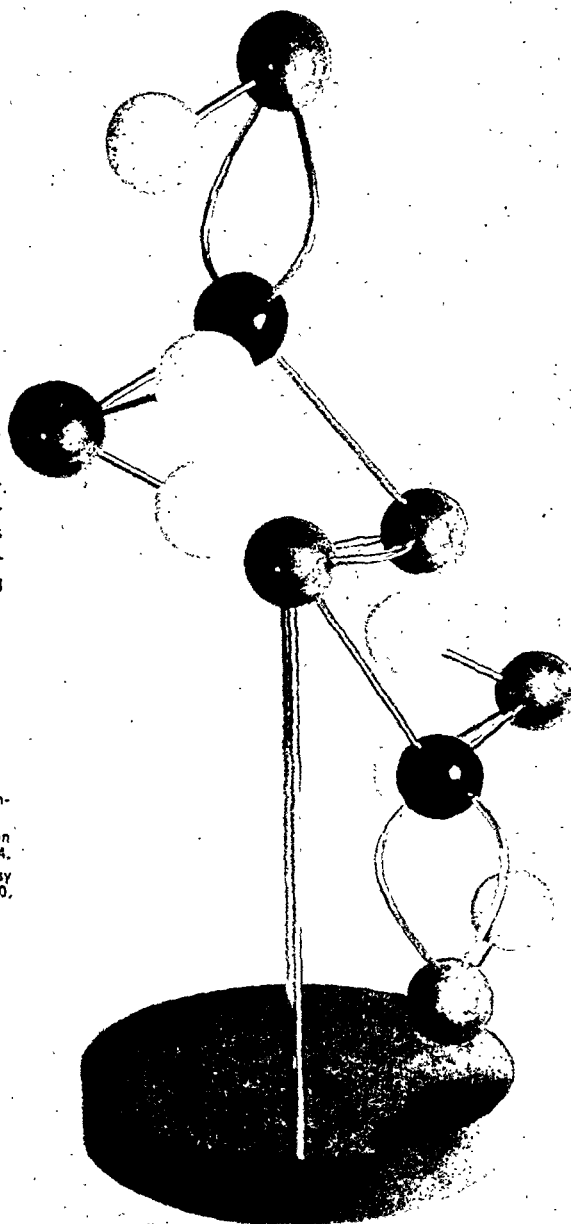
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